PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Edward J. Koeneman	Examiner:	Jonathan M. Foreman
Serial No.	10/727,212	Group Art Unit:	3736
Filed:	December 2, 2003	Docket No.	058482-010101
Customer No.:	33717	Conf. No.:	5429
Title:	SYSTEM AND METHOD FOR NEUROMUSCULAR REEDUCATION		

CERTIFICATE OF TRANSMISSION

I hereby certify that this document is being transmitted electronically to the United States Patent and Trademark Office via the EFS Web e-Filing system on July 27, 2009.

Kelly Simpson

Name: Kelly Simpson

DECLARATION OF JAMES B. KOENEMAN PURSUANT TO 37 C.F.R. § 1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, James B. Koeneman, Ph.D., having my business address at Kinetic Muscles, Inc., 2103 E. Cedar St. Suite 3, Tempe, AZ 85281, hereby declare:

1. I am a joint inventor, along with Edward J. Koeneman, Donald E. Herring, and Robert S. Schultz, of the subject matter claimed in the above-cited patent application entitled "SYSTEM AND METHOD FOR NEUROMUSCULAR REEDUCATION." Kinetic Muscles, Inc. is the assignee of this patent application.

2. I am familiar with the above-cited application. I am also familiar with the Office Action mailed April 1, 2009. I am aware that the Examiner has rejected the claims under 35 U.S.C. §102 and §103 as being obvious over McBean et al. (US 7,396,337) in view of Meyer

(US 5,012,820), Grove et al. (US 6,010,468), and Wood et al. (US 2002/0143277). The Examiner states that the McBean et al. reference discloses an orthotic device that detects signals from various EMG and joint position sensors on a patient's limb or body part and causes the patient's joint to move accordingly. I disagree with the Examiner's analysis of the references and conclusions. However, the McBean et al. reference is not applicable to our patent application, and I will discuss that issue below.

3. Our claimed invention, which is a system for assisting neuromuscular function that includes an EMG sensor, joint position sensor, computer processor for implementing a protocol, and motion causing device, was conceived and diligently reduced to practice prior to the earliest claimed priority date of November 21, 2002 of the McBean et al. reference. Since well before that date, I and my coinventors have been diligently testing, experimenting and perfecting the invention.

4. As proof of this fact, on March 29, 2001, I submitted a Small Business Innovation Research Program (SBIR) Phase I contract proposal "Development of a Massed Practice Stroke Therapy Device" to the National Institutes of Health (NIH). Exhibit A. The SBIR Phase I contract proposal confirms that I had conceived the key aspects of my invention as relevant to the McBean et al. reference well before November 21, 2002. For example, on page 14, the document illustrates that I had conceived a lightweight air muscle actuated device that incorporates EMG sensing, neuromuscular stimulation and joint position sensing. Furthermore, on page 15, the document describes a protocol where if an EMG signal is present but no motion from the patient occurs, the air muscle is stimulated and the joint is moved. If motion is also detected, the air muscle is triggered when the motion has stopped.

5. The NIH posed questions regarding our SBIR Phase I contract proposal, to which we responded with a revised SBIR Phase I contract proposal that was submitted to the NIH on November 30, 2001. A copy of the revised SBIR Phase I contract proposal is attached as Exhibit B.

6. The NIH posed further questions to which we responded with a second revised SBIR Phase I contract proposal submitted to the NIH on July 29, 2002. A copy of the second revision of the SBIR Phase I contract proposal is attached as Exhibit C.

7. We eventually obtained NIH funding in excess of $5 million for our company and for our clinical partners for development and testing of three devices covered by the pending application, for treatment of hand, foot and upper extremity conditions.

8. These March 29, 2001, November 30, 2001 and July 29, 2002 documents demonstrate that work on this project continued diligently since before the effective date of the McBean et al. reference. Our provisional patent application was filed on December 4, 2002.

9. Throughout this entire period, we continued to actively work on this project, including conducting a pilot study between about August 2002 through November 2002 to gather performance data. During the study we measured performance of the device and protocols, asked the participants to fill out questionnaires, conducted focus groups, etc. As a result of the study, we made changes to the device and protocols.

10. We also conducted tests on stroke patients with our device during this period, and eventually obtained FDA registration in 2003. We had begun our discussions with the FDA in early 2001. Clinical testing began in August 2002. The device which is the subject of the pending patent application, which we now call the Hand Mentor, was classified as a "Non Significant Risk" and, therefore, we did not need an Investigational Device Exemption (IDE) for testing of this device. We also received notification from the FDA that our device did not require a 510(K) application. We received our registration number from the FDA on May 28, 2003 (FDA registration no. 9056585).

11. In summary, we began development of our invention well before the effective date of the McBean et al. reference, and continued working diligently on its development up until we filed our provisional patent application on December 4, 2002 and our non-provisional patent application on December 2, 2003. By the time of the effective date of McBean et al., we had developed all of the major components of our invention as claimed in our pending patent application.

I further declare that all statements made herein of my own knowledge are true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the

United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issuing thereon.

James B Koeneman

James B. Koeneman, Ph.D.

7/24/2009

Date

Exhibit A

OMB No. 0925-0195
Expiration Date 8/31/2001

Department of Health and Human Services
Public Health Service

Small Business Innovation Research Program

Phase I Grant Application

Follow instructions carefully.

Leave blank — for PHS use only.		
Type	Activity	Number
Review Group		Formerly
Council Board *(Month, year)*		Date Received

1. TITLE OF APPLICATION *(Do not exceed 56 typewriter spaces)*
Development of a Massed Practice Stroke Therapy Device

2. SOLICITATION NO. **PHS 98-2**

3. PRINCIPAL INVESTIGATOR ☐ New Investigator

3a. NAME *(Last, first, middle)*
Koeneman, James Bryant

3b. DEGREE(S)
BSME | MS | PhD

3c. SOCIAL SECURITY NO. *Provide on Personal Data Page*

3d. POSITION TITLE
Senior Bioengineering Consultant

3e. MAILING ADDRESS *(Street, city, state, zip code)*
BTI Consultants
1937 East Broadway
Tempe, AZ 85282

3f. TELEPHONE AND FAX *(Area code, number, and extension)*
TEL: 480-967-1000
FAX: 480-967-4355

BITNET/INTERNET Address:
jbk@btic.com

4. HUMAN SUBJECTS
☐ NO
☒ YES

4a. If "yes," Exemption no. or IRB approval date: Pending
☐ Full IRB or ☐ Expedited Review

4b. Assurance of compliance no.

5. VERTEBRATE ANIMALS
☒ NO
☐ YES

5a. If "Yes," IACUC approval date

5b. Animal welfare assurance no.

6. DATES OF PROJECT PERIOD
From: Nov. 5, 2001 *Through:* April 30, 2002

7. COSTS REQUESTED
7a. Direct Costs $ 90,000
7b. Total Costs $ 100,000

8. PERFORMANCE SITES *(Organizations and addresses)*
BTI Consultants
1937 East Broadway Road
Tempe, AZ 85282-1701

Barrows Neurological Institute -
St. Joseph's Hospital
350 West Thomas Road
Phoenix, AZ

9. APPLICANT ORGANIZATION *(Name and address of applicant small business concern)*
BTI Consultants
1937 East Broadway
Tempe, AZ 85282

10. ENTITY IDENTIFICATION NUMBER
86-0411058

Congressional District
1

11. SMALL BUSINESS CERTIFICATION
☒ Small Business Concern ☐ Women-owned
☐ Socially and Economically Disadvantaged

12. NOTICE OF PROPRIETARY INFORMATION: The information identified by asterisks(*) on pages ______________ of this application constitutes trade secrets or information that is commercial or financial and confidential or privileged. It is furnished to the Government in confidence with the understanding that such information shall be used or disclosed only for evaluation of this application, provided that, if a grant is awarded as a result of or in connection with the submission of this application, the Government shall have the right to use or disclose the information herein to the extent provided by law. This restriction does not limit the Government's right to use the information if it is obtained without restriction from another source.

13. DISCLOSURE PERMISSION STATEMENT: If this application does not result in an award, is the Government permitted to disclose the title only of your proposed project, and the name, address, and telephone number of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information or possible investment? ☒ YES ☐ NO

14. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Name: Vaughn P. Adams, Jr., P.E., Ph.D.
Title: President and CEO
Address: BTI Consultants
1937 East Broadway
Tempe, AZ 85282

Telephone: 480-967-1000
FAX: 480-967-4355
BITNET/INTERNET Address:
vpa@btic.com

15. PRINCIPAL INVESTIGATOR ASSURANCE: I certify that the statements herein are true, complete, and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

SIGNATURE OF PERSON NAMED IN 3a *(In ink. "Per" signature not acceptable.)*
James B Koeneman

DATE
3/29/01

16. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete, and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Service terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF PERSON NAMED IN 14 *(In ink. "Per" signature not acceptable.)*
V Adams

DATE
3-29-01

Principal Investigator *(Last, first, middle)*: Koeneman, James Bryant

Abstract of Research Plan

NAME, ADDRESS, AND TELEPHONE NUMBER OF APPLICANT ORGANIZATION

BTI Consultants
1937 East Broadway Road
Tempe, AZ 85282
480-967-1000

YEAR FIRM FOUNDED	NO. OF EMPLOYEES *(include all affiliates)*
1981	Full time: 13 Part time: 14

TITLE OF APPLICATION

Development of A Massed Practice Stroke Therapy Device

KEY PERSONNEL ENGAGED ON PROJECT

NAME	ORGANIZATION	ROLE ON PROJECT
James B. Koeneman, Ph.D.	BTI Consultants	PI, Biomechanics
Christina Kwasnica, M.D.	Barrows Neurological Inst.	Clinical Requirements and Evaluation
Douglas Wendelboe	BTI Consultants	Firmware Design
Edward Koeneman	BTI Consultants	Electronic Design and Prototype Fabricator
Donald Herring	BTI Consultants	Industrial Design, Human Factors

ABSTRACT OF RESEARCH PLAN: State the application's broad, long-term objectives and specific aims, making reference to the health-relatedness of the project. Describe concisely the research design and methods for achieving these goals and discuss the potential of the research for technological innovation. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. *Therefore, do not include proprietary or confidential information.* DO NOT EXCEED 200 WORDS.

Stroke (CVA) is the leading cause of disability in the United States and it is estimated that its prevalence will more than double over the next 50 years. Current stroke therapy is labor-intensive and costly. The United States spends $17 billion taking care of stroke survivors. Recently, concentrated, massed practice therapies have been developed that improve function in CVA patients by reversing the effects of "learned nonuse". The objective of this project is to develop a device that facilitates the administration of massed practice stroke therapy. The long-term objective is to provide a lightweight device for home use that provides motion, biofeedback, and neuromuscular stimulation. Software will be developed that controls the function of the device and monitors patient progress and compliance. A pneumatic artificial muscle will be used to provide physical motion. This artificial muscle has many of the properties of human muscle. It is lightweight, flexible and has spring-like properties. This project will focus on treating wrist extensor weakness, however, the concept applies to all areas affected by motor impairment.

Provide key words (8 maximum) to identify the research or technology.

Stroke therapy, massed practice, EMG biofeedback, neuromuscular stimulation, rehabilitation, pneumatic artificial muscle.

Provide a brief summary of the potential commercial applications of the research.

This device will provide an economical means of administering massed practice stroke therapy. This device has the potential to provide effective treatment for other motor disabilities such as patients with traumatic brain injury, spinal cord injury, and hip fracture.

Budget Justification

Using continuation pages if necessary, describe the specific functions of the personnel and consultants. Read the instructions and justify costs accordingly.

James Koeneman, Ph.D., PI, will coordinate the project and be responsible for the biomechanical design issues and risk analysis. He will spend 30% of his time on the project.

Christina Kwasnica, M.D., will coordinate the clinical input to the design requirements and the clinical evaluation of the device.

Douglas Wendelboe will be responsible for firmware and electronic hardware design. He will spend 30% of his time on this project.

Donald Herring will be responsible for the design of the arm attachments and the human factors and industrial design issues. He will spend 15% of his time on the project.

Edward Koeneman will be responsible for construction and testing of prototypes. He will spend 30% of his time on the project.

Vaughn Adams will chair the Advisory Board and supervise the risk analysis. He will devote 10% of his time to the project.

The Advisory Board consultants are budgeted at $10,000.

Dr. He will consult on neuromuscular stimulation and EMG sensing.
Glen Stranton will consult on manufacturing issues.
Deborah Koeneman will consult on GMP and regulatory issues.
John Koeneman will consult on Phase III implementation.

The expenses at the Barrow Neurological Institute for patient evaluation studies in the last month of the project are budgeted at $10,000.

No fixed fee is requested.

Resources

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. (The research to be performed by the applicant small business concern and its collaborators must be in facilities that are available to and under the control of each party for the conduct of each party's portion of the proposed project.) Indicate their capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Include laboratory, clinical, animal, computer, and office facilities at the applicant small business concern and any other performance site listed on the FACE PAGE. Identify support services such as secretarial, machine shop, electronics shop, and the extent to which they will be available to the project. Use continuation page(s) if necessary.

BTI Consultants owns and/or leases approximately 11,000 square feet of office, laboratory and warehouse space. The facility houses offices, meeting rooms, lunch room, two shop areas, microscopy area, library and a computer lab. The library has an extensive collection of safety, human factors, and engineering books and industrial safety standards. All office computers are connected by a Novel Network and all have Internet access through a frame relay line. Receptionist, shipping/receiving, secretarial, facsimile, copying and technician assistance are available to this project.

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of each.

Approximately 1,000 square feet of office and prototype lab space have been exclusively allocated to this project. Video and 35 mm cameras, a large format color printer (36"), a 4x compact disk recorder, and various computer simulation programs and equipment, including AutoCAD, 3D Studio MAX, Photoshop, Illustrator, Character Studio, Speed Razor, Humanoid, Perception Video Capture, and Sound Forge, are available for use.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
James B. Koeneman	Senior Biomechanics Consultant

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Minnesota, Minneapolis, MN	BSME	1959	Mechanical Engineering
Case Western Reserve University, Cleveland, OH	MS	1966	Bioengineering
Case Western Reserve University, Cleveland, OH	PhD	1970	Structures/Mechanical Dcsign

RESEARCH AND PROFESSIONAL EXPERIENCE

1994 - present	Senior Bioengineering Consultant, BTI Consultants, Tempe, AZ. Assistive Devices, Biomechanics, Development of Composite Materials, Stress Analysis, Failure Analysis.
1994 - 1998	V.P. of Engineering, Orthologic Corporation, Tempe, AZ. Fracture fixation devices, bone growth stimulators.
1984 - 1994	Head of Bioengineering Division, Harrington Arthritis Research Center, Phoenix, AZ. Development of assistive devices, orthopedic implant design and testing, finite element analyses.
1981 - 1983	President, Paulson Medical Devices, Inc., Erie, PA. Development of fracture fixation devices and orthopedic implants.
1974 - 1981	Head of Bioengineering Division, Lord Corporation, Erie, PA. Development and manufacture of orthopedic implants. Composite material development.
1970 - 1974	Bell Telephone Laboratories, Columbus, OH. Development of Piezoelectric switching devices.
1960 - 1964	Reactor Engineer, U.S. Atomic Energy Commission, Argonne, IL.
1959 - 1960	Reactor Engineer, Argonne National Laboratory, Idaho Falls, ID.

PUBLICATIONS

Recipient of 16 patents, co-author of 22 publications and over 115 presentations at technical society meetings. Seven relevant publications listed below:

J.B. Koeneman and J.S. Kaiser, "A Functional Evaluation of the DataHand® Key Entry System User Experience Evaluated By Questionnaire," RESNA, 1994.

J.B. Koeneman and C. Eblen, "A Longitudinal Evaluation of Four-Wheeled Walker: Effects of Experience," Topics in Geriatric Rehabilitation, 8(3)3, 1993.

J.B. Koeneman, "Advanced Materials for Assistive Devices," Topics in Geriatric Rehabilitation, Vol. 8, No. 2, December 1992.

J.B. Koeneman, with others, "A Multi-Dimensional Evaluation of a Four-Wheeled Walker," Assistive Technology, Vol. 4, No. 1, 1992.

J.B. Koeneman, N. Reich, P. Otten, and J. Kaiser, "Clothing for Special Needs; An Information Arena," 10th Annual RESNA Conference, San Jose, CA, 1987.

J.B. Koeneman and M. Phillips, "Composite Materials for Rehabilitation Devices," 10th Annual RESNA Conference, San Jose, CA, 1987.

J.B. Koeneman, "State of the Art of Finite Element Analysis in Orthopaedics," Materials Research Society, Proceedings of Medical Devices and Materials Symposium, 1987.

AWARDS

International Fellow of Biomaterials Science and Engineering; International Union of Societies for Biomaterials Science and Engineering (1999)

Clemson Award for Contributions to the Literature, Society for Biomaterials (1997)

Fellow of Society for Advancement of Material and Process Engineering International (SAMPE) (1992)

Chapter Fellow Award, Society for Advancement of Materials and Process Engineering (SAMPE) (1990)

Engineer of the Year Award, Erie Engineering Society Council (1982)

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Christina M. Kwasnica, M.D.	Director of Brain Injury Rehabilitation

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Arizona, Tucson, AZ	BA	1991	Political Science
Northwestern University Medical School, Chicago, IL	MD	1995	Medicine

POSITIONS

2000-Present Director of Brain Injury Rehabilitation Barrow Neurological Institute, Phoenix, AZ

1999-2000 Clinical Instructor and Cognitive Neurology Fellow, Northwestern University Alzheimer's Disease Center, Departments of Neurology and Physical Medicine and Rehabilitation, Chicago, IL

1995-1999 Resident Physician, Northwestern University Medical School/Rehabilitation Institute of Chicago, Department of Physical Medicine and Rehabilitation, Chicago, IL

PROFESSIONAL AFFILIATIONS

Diplomate, American Board of Physical Medicine and Rehabilitation

Fellow, American Association of Physical Medicine and Rehabilitation

Diplomate, Association of Academic Physiatrists

AWARDS AND HONORS

Seabury Foundation Endowed Research Resident, July 1998-June 1999

NIH National Research Service Award Fellowship, F32 NS10858-01, August 1999-August 2000

Sara Baskin Award for Research Excellence, Rehabilitation Institute of Chicago, May 1999

President's C62nd Annual, 2nd Annual Assembly of the American Academy of Physical Medicine and Rehabilitation, for outstanding paper presentation, "Predictors of Ambulation in Stroke Rehabilitation"

RESEARCH PROJECTS ONGOING OR COMPLETED DURING THE LAST THREE YEARS

Current Predictors of Ambulation in Stroke Rehabilitation with Dr. Richard Harvey, Rehabilitation Institute of Chicago

Pending Unilateral Neglect and the Relationship of Measurements with Function

Prior Bromocriptine in Unilateral Neglect- F32 NS10858-01

NIDRR Stroke Research and Training Center- Rehabilitation Institute of Chicago

PEER REVIEWED PUBLICATIONS

Kwasnica, C.M. and Heinemann, A. "Coping with Traumatic Brain Injury: Representative Case Studies," Archives of Physical Medicine and Rehabilitation, April 1994, pp. 384-389

Grujic, Z., Mapstone, M., Gitelman, D., Weintraub, S., Johnson, N., Hays, A., Kwasnica, C.M., Harvey, R.L., and Mesulam, M. "Dopamine Agonists Reorient Visual Exploration Away from Neglected Hemisphere," Neurology, December 1998

Kwasnica, C.M. "Unilateral Neglect after Right Hemisphere Stroke- a Review of the Syndrome and Management," Critical Reviews in Physical Medicine and Rehabilitation, accepted for publication December 2000

SELECTED RECENT ABSTRACTS AND PRESENTATIONS

Kwasnica, C.M., Harvey, R.L., and Mullarkey, C. "Predictors of Ambulation in Stroke Rehabilitation," Presented at the America Academy of Physical Medicine and Rehabilitation annual meeting, November 2000

Kwasnica, C.M., Cherney, L., and Harvey, R.L. "Unilateral Neglect and Relationships with Functional Outcomes," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November 1998

Kwasnica, C.M., Grujic, Z., Mapstone, M., and Harvey, R.L. "Bromocriptine Effect on Unilateral Visual Neglect After Right Hemisphere Infarct: A Pilot Study," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November 1997

Managing Neglect Syndrome after Stroke: A Complete Experience- Annual Assembly of the American Academy of Physical Medicine and Rehabilitation, November, 1998

Managing Neglect Syndrome after Stroke: A Complete Experience- Annual Multidisciplinary Stroke Course- Rehabilitation Institute of Chicago, April 1999

Pharmacology of Brain Injury- Rehabilitation Institute of Chicago, December 2000

Non-traumatic Brain Injury- Rehabilitation Institute of Chicago, December 2000

Pharmacologic Approaches to Motor Recovery after Stroke- Annual Multidisciplinary Stroke Course- Rehabilitation Institute of Chicago, April 2000

Atypical Dementias- Grand Rounds- Ingalls Hospital- Chicago, IL, April 2000

Neuroplasticity and Rehabilitation- Grand Rounds- Rehabilitation Institute of Chicago, July 2000

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Douglas E. Wendelboe	Software Consultant; President, Penn Microsystems

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Pennsylvania State University, State College, PA	BS	1972	Electrical Engineering
University of Pennsylvania, Philadelphia, PA	MS	1976	Electrical Engineering

RESEARCH AND PROFESSIONAL EXPERIENCE

1998-Present Software Consultant, BTI Consultants, Tempe, AZ. Design of hardware and software for medical devices

1981-Present President, Penn Microsystems. Consulting on microprocessor-based products. Medical device projects include:

- Hand-held Blood Prothrombin-Time Measuring Device, San Jose, CA, 2000-Present
- Designed and implemented the Automated Calibration and Test System for the Bone Growth Stimulator, Phoenix, AZ, 1999-2000
- Firmware enhancements for an electromagnetic Bone Growth Stimulator, Phoenix, AZ, 1997-1999
- Developed an Automated Active Burn-In System for the Bone Growth Stimulator, Phoenix, AZ, 1996-1997
- Designed and implemented firmware for Nerve Integrity Monitor Instrument, Jacksonville, FL, 1994-1995
- Designed, implemented, and maintained the firmware for a line of Micro-titer Plate Readers, Winooski, VT, 1982-1985
- Designed and implemented the complete firmware for a Pacemaker Systems Analyzer, Winooski, VT, 1980-1981

1977-1981 Senior Associate Engineer, IBM Corp., Essex Junction, VT

1976-1977 Senior Product Engineer, Honeywell Corp., Ft. Washington, PA

1972-1976 Design Verification Software Engineer, UNISYS (Sperry-Univac), Blue Bell, PA

PROFESSIONAL PUBLICATIONS

"Recommended Use of the PL/M Computer Language in Safety-Related Systems," Report for the Nuclear Regulatory Commission, NUREG/CR-6463, June 1996

Co-publisher of the Annual "Arizona High Tech Directory"

Columnist for the "Arizona High Tech Times" newspaper

PROFESSIONAL

IEEE Computers, IEEE Software, IEEE Management, IEEE Biomedical

American Society for Quality

TECHNICAL SKILLS

Languages: Keil C51 w/uVision2, IAR C, PIC-C, 8051, 8x86, 68xx, 68xxx assembler, Microchip PIC, Hitachi H8 assembler, TMS320C54x Algebraic assembler, National Instruments LabWindows/CVI, Microsoft Visual C++, Visual Basic

RTOS: uC/OS-II, QNX, Keil RTX-51, familiarity with VxWorks, Tornado

Microprocessors: Intel 8051, 80251, 8X93x USB, Intel 80x86, 80188, 386EX, 68HC05, 68HC08, 68HC11, 68xxx family, Hitachi 6303, H8S/2134, Microchip PIC16C74, 16C65, ST Micro ST10F167/168

In-Circuit Emulation: Intel ICE 8051, 8085, 80188, 80x86, Nohau EMUL51-PC: 80C552, 89C51RD2, Microchip PIC-Master & others

Peripheral Buses: I^2C, CAN v2.0, USB, Motorola SPI, Dallas Semiconductor interfaces

Design Standards: IS)-9001 Design Quality Standards, FDA (97-4179) Medical Device Quality Systems Standards, FDA 510(k), FDA Pre-Market Approval (PMA)

Bus Boards: PC/104 Bus, STD Bus, VME Bus

Logic: SPICE Simulation, Programmable Logic Compilers

Network: TCP/IP, WATTCP

Database: MS SQL7, Oracle, Informix

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Edward J. Koeneman	Consultant

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Arizona State University, Tempe, AZ	BSEET	1992	Electronic Engineering
Arizona State University, Tempe, AZ	MT	1994	Electronic Engineering

POSITIONS

1999-Present	BTI Consultants, Consultant.
1997-1999	Adtron Corp., Mesa, Arizona. Product Manager, Data Storage Devices.
1997	PCI Medical, Phoenix, Arizona. Design Engineer, Medical Electronics.
1995-1997	Prescom Electronics, Mesa, Arizona. Chief Engineer, Contract Electronic Design and Manufacturing.
1988-1995	Harrington Arthritis Research Center, Phoenix, Arizona. Lab Coordinator for Orthopaedic Resident Projects, Mechanical Testing.

PEER REVIEWED PUBLICATIONS

Koeneman, E.J., J.A. Lerman, R.J. Haynes, J.B. Koeneman, W. B. Wong, "A Biomechanical Comparison of Gardner-Wells Tongs and Halo Device Used for Cervical Spine Traction," SPINE, Volume 19, Number 21, pp. 2403-2406, 1994.

Koeneman, E.J., N.R. Crawford, A.G.U. Brantley, C.A. Dickman, "An Apparatus Applying Pure Nonconstraining Moments To Spine Segments In Vitro," SPINE, Volume 20, Number 19, pp. 2097-2100, 1995.

SELECTED PRESENTATIONS

Koeneman, E.J., J.A. Lerman, J.E. Maisel, J.B. Koeneman, "Electromyographic Analysis of the Hockey Slapshot," Presented at 1994 Fall Meeting of the Biomedical Engineering Society.

AWARDS AND HONORS

IEEE Outstanding Student Achievement Award, 1993

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Donald E. Herring	Senior Industrial Design Consultant

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
American University, Washington, DC	BA	1967	Govt. and Public Admin.
Arizona State University, Tempe, AZ	BS	1982	Product Design
Arizona State University, Tempe, AZ	MSD	1993	Human Factors and Design

PROFESSIONAL EXPERIENCE

2001-Present	Senior Industrial Design Consultant, BTI Consultants, Tempe, Arizona
1998-Present	Assistant Professor, Arizona State University, Tempe, Arizona
1997-1999	Proprietor, Redfish Design, Phoenix, Arizona
1994-1997	Assistant Professor, Purdue University, West Lafayette, Indiana
1992-1994	Exhibit and Industrial Designer, Sunbelt Scenic Studios, Inc., Tempe, Arizona
1991-1992	Exhibit Designer, Giltspur Exhibits, Phoenix, Arizona
1982-1989	Senior Project Designer, Mattel Toys, Hawthorne, California
1975	Arizona Real Estate Sales and Brokerage, Phoenix, Arizona
1973	Specialist, United States Treasury Department, Washington, D.C.
1972	Foreman, Athens Paint & Drywall Company, Alexandria, Virginia
1968	OJT Contract Writer, Washington Urban League, Washington, D.C.
1968	Capitol Policeman, United States Capitol Building, Washington, D.C.

PRINCIPAL PROFESSIONAL PUBLICATIONS AND PRESENTATIONS

"Children's Computer Human Factors and Seating Recommendations" (For Our Greatest Future Resource), Natural Resources, 1995 IDSA Design Education Conference Proceedings, Santa Fe, New Mexico, September 1995

"Twenty Years Later: What Are the 11982 Graduates of an Industrial Design Program Doing in the New Millennium?," Gumbo, 2000 IDSA Design Education Conference Proceedings, New Orleans, Louisiana, September 2000

MEMBERSHIPS IN SCIENTIFIC AND PROFESSIONAL SOCIETIES

Human Factors and Ergonomics Society of America
Arizona Chapter Member of the Human Factors and Ergonomics Society of America
Industrial Design Society of America (IDSA)
The Arizona IDSA Chapter Secretary (Founding member and officer)
The Indiana IDSA Chapter Secretary/Treasurer (Resigned, April, 1997)

PATENTS

U.S. Patent 4,787,876 - Toy Musical Play Set, 11/29/88, assigned
U.S. Patent 4,673,373 - Transformable Toy Block, 6/16/87, assigned
U.S. Patent 4,645,471 - Busy Ball Child's Toy, 3/7/85, assigned

AWARDS, SCHOLARSHIPS AND HONOR SOCIETIES

Netherlands Toy of the Year Award to Disney Pots and Pans Band based on Originality, Safety and Suitability, 1988

Second Place Award ($2,000.00) in Mattel's Toy of the Year Contest for the Invention and Development of the Double Dooz Transformers Toy Line, 1986

Nominated for the Mattel Toys Presidents Award for Leading a "Brainstorming Event" with 40 Participants Producing 100 Product Concepts for Presentation in Ten Days, 1985

Mattel $2000.00 Discretionary Award for "The First Innovative Preschool Product Line to Come out of Mattel in Eight Years," 1985

Arizona State University Outstanding Senior Industrial Design, 1982

Honorable Mention ($250.00) in Mattel Toy Design Contest, 1982

Awarded Internship at Mattel Toys, 1982

Phi Kappa Phi National Honor Society, 1982

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Vaughn P. Adams, Jr., Ph.D.	Senior Consulting Engineer

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Arizona State University, Tempe, AZ	BS	1964	Engineering Design
Arizona State University, Tempe, AZ	MS	1970	Human Factors Engineering
Texas A & M University, College Station, TX	PhD	1975	Safety Engineering

CONSULTING AND PROFESSIONAL EXPERIENCE

1980 - present Senior Consulting Engineer, President, C.E.O., BTI Consultants, Tempe, AZ. Human Factors Engineering, Systems and Product Design, Man/Machine System Integration, Product and Mechanical Design (including Defect and Patent Analysis), Consumer Product Risk Analysis, Hazard Quantification in Product and Systems Design, Systems Safety Engineering, System Safety Quantification Techniques such as Failure Mode and Effects Analysis, Fault Tree Analysis, Hazard Analysis, Biostereometric Applications to Physical Anthropometry, Forensic Engineering, Occupational Health and Safety Engineering.

1973 - 1980 Professor, Chairman, Department of Design Science, Arizona State University, Tempe, AZ.

1972 - 1973 Sabbatical to Texas A & M University, College Station, TX.

1964 - 1972 Lecturer to Assistant Professor, Arizona State University, Tempe, AZ.

PROFESSIONAL SOCIETIES

Society of Automotive Engineers (Member)
American Society of Engineering Education (Member)
Society of Manufacturing Engineers (Senior Member)
Society of American Value Engineers (Member)
Human Factors Society (Member)
American Institute of Industrial Engineers (Member)
American Society of Safety Engineers (Professional Member)
National Academy of Forensic Engineers (Fellow) #68F
System Safety Society (Member)
National Society of Professional Engineers (Member)
Society of Professional Engineers - Arizona (Member)
Society of Professional Engineers - Texas (Member)
Arizona Council of Engineering and Scientific Associations (Member)
American Society of Testing and Materials (Member)
American National Standards Institute (Member)
American Society of Agricultural Engineers (Member)
Human Factors and Ergonomics Society (Member)

HONORS

ASEE-NASA Faculty Research Fellowship, Stanford University, Ames Research Center (1980)
ASEE-NASA Faculty Research Fellowship, University of Houston, Johnson Space Center (1976-77)
Alpha Pi Mu (National Industrial Engineering Honor Society) Texas A & M University (1973)
Psi Chi (National Psychology Honor Society) Texas A & M University (1973)
ASEE-NASA Summer Faculty Fellowship Program in Systems Design, Stanford University (1968)
Graduation with Distinction, Arizona State University, College of Engineering Sciences (1964)

RESEARCH PLAN

A. SPECIFIC AIMS

The overall purpose of this project is to improve the restoration of physical function of stroke patients by incorporating into one device, three treatment modalities (massed therapy, neuromuscular stimulation, and biofeedback) that individually are successful in treating stroke patients. The device will provide cost effective therapy by supplying more information to the physician and therapist while reducing the amount of patient contact time. The device will be adaptable to accommodate the changing paradigm of cardiovascular accident or stroke (CVA) rehabilitation service delivery and to assist in studies designed to refine therapy protocols.

The specific aims of this proposal are:

1. Define the specific clinical information and display format that supports effective physician and therapist evaluation.
2. Write firmware to control, record, and display device function.
3. Design and fabricate a small, lightweight, portable control and patient-monitoring module.
4. Optimize the pneumatic system to provide a power source that allows therapy to continue during activities of daily living.
5. Fabricate and supply a prototype device for clinical testing.

B. SIGNIFICANCE

Many people have movement disabilities caused by disease or injury. Among the causes are CVA, traumatic brain injury, multiple sclerosis, spinal cord injury and Parkinson's disease. This project focuses on stroke. However, the results will have application to other causes of movement disability. Stroke is the leading cause of disability in the United States with at least 700,000 new cases each year [1, 2, 3]. Over half of these people have residual physical disability. Current stroke therapy is labor-intensive and costly. Often insurance does not cover the cost of full therapy. One estimate is that the United States spends $30 billion a year to take care of stroke survivors. Seventeen billion dollars of this is direct medical cost and thirteen billion is indirect cost due to lost productivity [3]. Another estimate is that the total direct and indirect costs of stroke are $43.3 billion per year [3]. The number of strokes is projected to increase due to the increase in the over 50 "baby boom" population. Also, new pharmaceutical treatments for stroke are projected to increase the number of patients surviving a stroke and increase the percentage of stroke victims requiring rehabilitation. A recent estimate is that the prevalence of stroke will more than double over the next 50 years [2].

Historically, therapy for CVA patients has concentrated on helping a patient adapt to their disability. This methodology is reinforced by the reduction in covered rehabilitation services. It has been shown that this treatment leads to "learned nonuse" that hinders the restoration of available function [2]. Animal studies suggest that learned nonuse is established by the initial organic damage. A patient is

punished for trying to use the affected limb and is rewarded for using other parts of the body. Over time, healing of the organic damage occurs but the suppression of use learned in the acute phase remains in force [4]. Recently, concentrated therapies have been developed that improve function in CVA patients by reversing the effects of "learned nonuse" [4]. As discussed by Taub [4], many of the therapies that have been shown to be effective in restoring function involve massed practice. Physical therapy training techniques were used by Bach-y-Rita [5, 6] and Franz, Scheetz, and Wilson [7]. Significant improvement in limb function was obtained in chronic CVA patients. Training techniques based on electromyography (EMG) biofeedback improved motor ability of chronic CVA patients in studies by Wolf [8, 9], Basmajian [10, 11], and Balliet [12]. Repetitive concentrated practice produced large therapeutic effects for lower limb function [13, 14, 15]. Taub has thoroughly studied Constraint-Induced (CI) Movement Therapy [2, 32]. His group has shown positive results in controlled randomized studies [16]. Some of these experiments compared several massed therapy techniques and all showed very large increases in limb use over the treatment period.

Two very sophisticated robot systems are being developed for treatment and evaluation of CVA patients [1, 17]. These devices have shown some effectiveness in treatment of CVA patients and have developed very useful data for understanding recovery mechanisms. However, the current cost of these systems preclude their widespread clinical use [18].

Studies show that EMG triggered neuromuscular electrical stimulation is effective in restoring function to CVA patients [26, 27, 28, 29]. However, the discomfort of surface neuromuscular stimulation significantly limits the clinical implementation of this modality for persons with hemiplegia [34]. Low-intensity neurostimulation (stimulation that increases a patient's voluntary range of motion without producing any visible movement at rest) also is effective [28]. This level of stimulation is much more tolerable. Although gross muscle contraction is not produced by low-intensity stimulation, voluntary contraction might be more functional since the flexor/extensor activity of the extremity is better balanced [28]. Low-intensity electrical stimulation has effects similar to functional electrical stimulation except for the lack of motion proprioception. The purpose of the device used in our program is to provide this information with passive motion and combine it with EMG stimulated low-intensity electrical stimulation.

EMG biofeedback treatment of stroke patients has shown some success [30, 31, 12, 8]. This treatment uses surface electrodes to capture the electrical activity of a selected muscle group. An electronic unit converts the signals into visual or audio information for the patient. This information is used by the patient to augment or decrease muscle activity.

A device that has a venerable history in supplying motion to assistive devices is the pneumatic artificial muscle. The artificial muscle exhibits many of the properties of human muscle. The device consists of an expandable internal bladder, e.g., a rubber tube, surrounded by a braided shell. When the internal bladder is pressurized, it expands radially against the braided shell. The pressure on the inside of the braid causes it to contract. Braided finger traps used to hold fingers on therapy devices contract radially when pulled. The air muscle works in the same manner only in the opposite direction, i.e., increasing the diameter causes it to shorten. Like human muscle, the device has spring-

like characteristics, is flexible, and is lightweight. The force-deflection characteristics can be made similar to those of human muscle. This type of device was first used in the 1950s for powered braces [19, 20]. Pressurized air canisters or accumulators that are recharged by air compressors supply air. A major advantage of the air muscle is that it is flexible and can be easily adapted to address the specific loss of function exhibited by a patient. Many refer to this type of device as the McKibben Artificial Muscle. The device has three times the pull force of an air piston of the same cross sectional area. The potential of this device is because it is low cost, lightweight, has a low profile, and has low noise operation. It has not been used extensively because it has been applied in the wrong applications and lack of engineering in critical areas. Research on the application of the air muscle has been revived by the University of Washington [21, 22, 23, 24, 25]. The Shadow Organization in England uses the air muscle to operate biped and multiped robots [33].

The labor-intensive and long treatment times of massed practice make effective rehabilitation expensive. A promising approach to providing a lightweight, low-cost stroke therapy device is a system that synergistically combines three modes of treatment that individually have been shown to be effective (massed practice, electrical neuromuscular stimulation, and biofeedback). We have constructed a laboratory-based prototype of an air muscle powered therapy device that has the adaptability to be used in current treatment modalities and also in the refinement of rehabilitation methods. We attached an artificial muscle between the proximal forearm and a hook on the proximal-dorsal region of the hand. A data acquisition board (Data Translation) and software (LabTech Notebook) were used with a Pentium computer to control an air valve to the muscle and record wrist extensor EMG and wrist position. Images Company, Staten Island, NY, supplied the wrist position sensor. The air tank supplying the muscle was kept at pressure by a compressor. The PC-based system is useful for the development of control and recording strategies. The EMG sensor feeds back information to the patient to reinforce when wrist extensors are active. The EMG signal can also be used to trigger passive motion using the artificial muscle and to provide neuromuscular stimulation. The purpose of this proposal is to transform this PC-based prototype into a self-contained patient-wearable device that records and later displays patient performance.

C. RELEVANT EXPERIENCE

The principal investigator for this development project is Dr. James Koeneman. Dr. Christina Kwasnica is the clinical co-investigator. Douglas Wendelboe and Edward Koeneman are the engineering co-investigators. Dr. Koeneman is responsible for coordination of the project and also for the design, analysis, and characterization of the artificial muscle. Doug Wendelboe is responsible for electronic hardware and firmware design. Ed Koeneman is responsible for fabrication and testing of the prototypes. Don Herring is responsible for human factors considerations and industrial design. Dr. Vaughn Adams will coordinate project evaluation by chairing the Advisory Board and will provide system safety guidance. The qualifications of the investigators are listed below.

Principal Investigator

Dr. Koeneman has over 25 years experience in bioengineering and biomechanics research and development. He started the bioengineering division of a private company. He also was the Vice President of Engineering for a publicly held company that manufactured fracture-healing devices. He managed the Assistive Devices Program at the Harrington Arthritis Research Center. He was elected a Fellow of the Society for the Advancement of Materials and Processing Engineers (SAMPE), received the Clemson Award for contributions to literature from the Society for Biomaterials for his work on the application of composite materials to medical devices, and was elected an International Fellow of Biomaterials Science and Engineering. He has performed analysis and testing of products for many medical device companies. He has 16 patents on medical devices.

Co-Investigators

Dr. Kwasnica is the Director of Brain Injury Rehabilitation at the Barrow Neurological Institute in Phoenix, AZ. The Barrows Institute is part of St. Joseph's Hospital and Medical Center and is well known for its neurological treatment and research. Dr. Kwasnica has been involved in stroke and traumatic brain injury research at the Rehabilitation Institute of Chicago and at the Barrows Institute. She is a Diplomate of the American Board of Physical Medicine and Rehabilitation, the Association of Academic Physiatrists, and a Fellow in the American Association of Physical Medicine and Rehabilitation.

Doug Wendelboe has over 25 years experience with software, firmware, and embedded circuit design. He has developed numerous innovative and well-documented firmware controlled systems for medical devices in accordance with FDA Design Control Procedures. His systems used sensor measurements to control device performance. They included internal calibrations and stored clinical performance for later review by physicians. Don Herring is an experienced Industrial Designer and is currently doing research and teaching classes in a joint program between the Departments of Bioengineering and Industrial Design at Arizona State University (ASU). He is experienced in Human Factors and Person-Machine research. Ed Koeneman has a Master's Degree in Electrical Engineering Technology from ASU and has been testing medical devices and assisting orthopaedic residents with research projects for over 10 years. He developed a telemetry surface EMG system for one of the projects. Dr. Vaughn Adams, the president of BTI Consultants, has over 35 years experience in design, human factors, and system safety engineering. He will chair the advisory board and also consult on the design to insure that system safety is considered during the total design process.

D. EXPERIMENTAL DESIGN AND METHODS

This design project is being done in accordance with Design Control Procedures established by the Food and Drug Administration (FDA). Important parts of Design Control Procedures are to: establish **design requirements**, document a **project plan**, keep a design history file, develop **design specifications** that meet the design requirements, **verify and validate** the design, and have design

reviews at the end of specified design stages. Our PC-driven prototype device will be the starting point for the development program.

Design Requirements

Based on discussions with clinicians and a review of the stroke therapy literature, the need was identified for a simple, low-cost device that could provide massed therapy without requiring continuous therapist attention. Preliminary design brainstorming suggested that the device should incorporate two other effective modalities: biofeedback and electrical neuromuscular stimulation. The Design Characteristics for this design are shown in Table I. During Phase I, these Characteristics will be translated into more quantitative Design Requirements. The Advisory Board that consists of experienced engineers and clinicians will approve the final Design Requirements.

TABLE I: DESIGN CHARACTERISTICS

- The device will provide massed practice, low level neuromuscular stimulation, and EMG biofeedback.
- The device will be sufficiently lightweight so that the patient is comfortable using it for long periods of time.
- Patient compliance will be recorded and available for display at therapist follow-up visits.
- Patient function history will be recorded and available for display at therapist follow-up visits.
- The patient will be able to perform activities of daily living while wearing the device.
- Human Factors considerations will be emphasized during the design process to assure ease of use, patient comfort, and patient compliance.
- A formal Risk Analysis will be prepared during the design process.
- The reliability and maintainability of the device will be considered in the design. The final design will be evaluated for robustness and maintainability.
- The device will be developed under the guidance of Medical Device Design Control Procedures.

Design Specifications

A device to treat wrist extensor weakness was selected as the first application. The PC-based prototype demonstrates that a lightweight air muscle actuated device can be made that incorporates EMG sensing, neuromuscular stimulation, and joint position sensing. During Phase I the functions performed by the general-purpose data acquisition and control software will be translated into specific firmware for a microprocessor that will be worn by the patient. The firmware will be written in blocks with verification of the functioning of each block determined during the writing of the code. All code will be written in accordance with the FDA guidelines for embedded firmware. The code will be fully documented and verified.

The circuitry for the EMG sensor, position sensor, local display, and neuromuscular stimulator will be redesigned and incorporated into one compact unit. The effect of electromagnetic radiation on the functioning of this device will be considered and the radiation generated by the device that could affect other devices will be measured. The design will be completely documented. Once a final design is completed, all specifications and drawings will be approved according to the Document Control System and any changes documented by change orders.

The device will provide the clinician flexibility on treating an individual patient. A basic case would be to have the sequence of events controlled as follows. The patient is instructed to try to extend the wrist when a beep is heard. The EMG sensor and the position sensor are monitored. If an EMG signal is present but no motion occurs, the neuromuscular stimulator and the air muscle are stimulated. If motion is also detected, we will wait until motion has stopped and then trigger the air muscle and apply neuromuscular stimulation. If neither motion nor an EMG signal is sensed, we will wait a period of time, say five seconds, and then trigger the air muscle and neuromuscular stimulation. Full extension will be held for about five seconds and then released. After the displacement has returned to the normal flexion position, we will wait another five seconds, then provide a beep, and the cycle starts all over. The clinician will be provided with basic sequences and triggering modes to choose from and also given the ability to custom design a treatment sequence.

Device attachments, biofeedback, and clinician display will be developed with significant Industrial Design and Human Factors input and review. Based on work with the prototype construction, a rendering of the final configuration of the device is shown in Figures 1 and 2.

Project Plan

Figure 3 is a Gantt chart of the Phase I tasks. The detail specifications of the firmware will be developed in the first month and code written and tested during the rest of the grant period. Selection of hardware components and circuit design begins at the start of the project and continues for four months. Fabrication of prototype boards begins after two and a half months and continues to the end of month five. Selection of suppliers for braid and rubber tubing and finalization of material specifications will be completed by the end of the first month. Mechanical performance of muscle designs will be measured in months two through five. Design of our own surface EMG sensor circuit and electrical stimulating circuit will begin at the start of the project and continue though the end of month five. The characterization of the sensor output will be done in month five. The final selection of the wrist position sensor model will be done in the first month and calibration completed in the second month. Hazard identification and risk analysis will be continuous through all design stages while the final hazards report will be written in month six. The assembled mobile prototype will be completed in the sixth month and tried on subjects with normal muscle function. Once the device performance has been evaluated, the device will be placed on CVA patients with wrist extensor weakness. Comfort and ease of use will be assessed in month six. During the final two months of the project, the final report and Phase II application will be written.

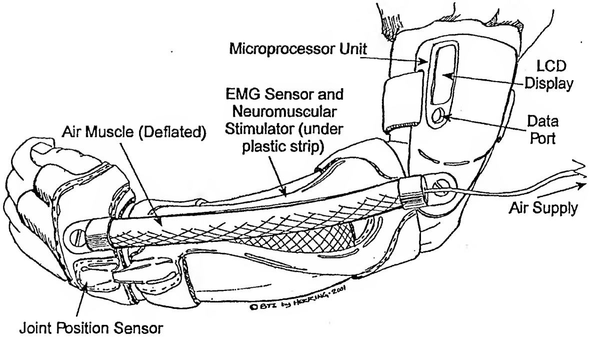


Figure 1 - Flexed Position

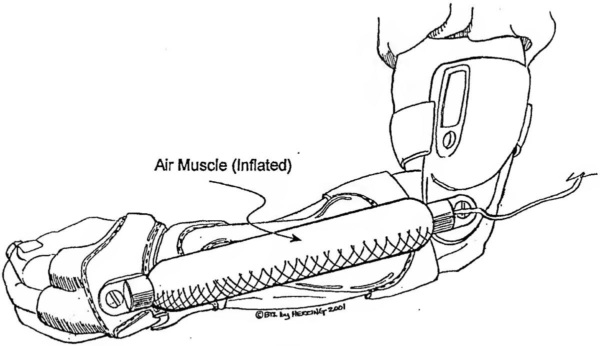
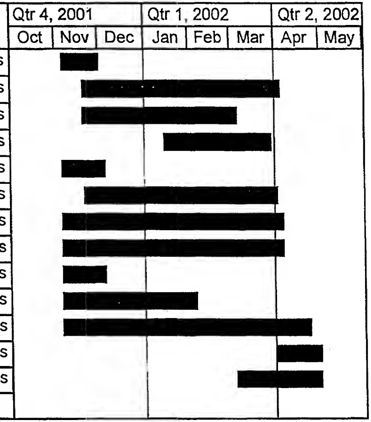


Figure 2 - Extended Position

FIGURE 3
GANTT CHART – PHASE I TASKS

ID		Task Name	Duration
1		Detail Firmware Specs	20 days
2		Write Firmware Code	98 days
3		Hardware Design	76 days
4		Hardware Fabrication	54 days
5		Artif. Muscle Material Sel	22 days
6		Muscle Characterization	95 days
7		Pneumatic Circuit Design	110 days
8		EMG Sensor Charact.	110 days
9		Wrist Position Sensor Char	22 days
10		Attachment Optimization	66 days
11		Risk Analysis	122 days
12		Subject Evaluation	22 days
13		Final Rept & Phase II Appl	42 days



In Phase II a controlled randomized clinical trial will be designed and implemented. CVA patients with chronic motor deficit will be treated with massed practice using this device and the restoration of their motor function will be compared to a similar patient group that undergoes the current standard Barrows CVA therapy. Phase II will also refine manufacturing methods.

Verification and Validation

A Failure Modes and Effects Analysis (FMEA) will be completed by the end of Phase I. This FMEA report is the synthesis of all of the design, testing, and information received during Phase I. All components and how they might fail are considered. Failure modes include the method of securement as well as physical failure of the device. The effects will examine the potential for injury to the patient. To do this analysis, the design during normal patient treatment and under foreseeable misuse must be included. This method establishes a matrix which relates system components to the applicable hazards, effects, severity, frequency, criticality, detection methods, and methods of compensation.

The feasibility of the device developed in Phase I will be evaluated by the criteria listed in Table II. The method of evaluation used to evaluate each is also listed.

TABLE II
PHASE I FEASIBILITY EVALUATION

Characteristic to be Evaluated	*Method of Evaluation*	*Criteria for Feasibility*
Safely control wrist motion	Risk Analysis; quantification of wrist function Range of Motion (ROM)	Risk is determined to be reasonable and acceptable. ROM from 90° flexion to 60° extension for a flaccid wrist
Monitor, record, display, and provide biofeedback of wrist motion and surface EMG signals from wrist extensors	Observation and final evaluation of functioning of the device. Inspection of calibration curves for EMG and wrist position sensors	Verification testing shows the device met the design requirements
Apply comfortable neuromuscular stimulation	Questionnaire administered to subjects	No evaluation greater than mildly uncomfortable
The device is portable and allows activities of daily living during treatment	Questionnaire administered to subjects	Response indicates subjects have mobility during treatment

E. HUMAN SUBJECTS

The use of the device on human test subjects and patients will occur in the final month of the project.

1. Involvement of human subjects: In the final month of the program the device that is developed will be tried on personnel involved in the development of the project. In addition, one or two patients that have wrist extensor weakness will be recruited to try the device in the clinic. An exclusion will be patients with spastic extensors. Clinicians will evaluate fit and comfort and the subjects will be given a questionnaire to complete.
2. Human Research Material: No human specimens or records will be used or recorded except for the response of test subjects to the device.
3. Recruitment of Subjects: Personnel involved with the development of the device will be the first subjects. Clinicians at Barrow Neurological Institute will recruit one or two CVA patients with wrist extensor weakness. This study will be submitted to the Barrows Institute Review Board (IRB). The purpose of the device and any risks involved by use of the device will be explained to the subjects and they will be required to sign a patient consent form that was approved by the IRB.
4. Risks: All hazards associated with use of the device will be identified in the Risk Analysis.
5. Minimization of Risk: Means of controlling the hazards identified in the Risk Analysis will be incorporated into the device design.
6. Reasonableness of Risk: The reasonableness of the risk in relation to the anticipated increase in function will be evaluated in the Risk Analysis.
7. FDA Approval: It is our opinion that this device is not a significant risk device. We will submit the protocol, a description of the device, a patient consent form, and an evaluation of the hazards involved in use of the device and how we are controlling these hazards to the Barrows IRB. If the IRB agrees with us that the device is not a significant risk, then an Investigational Device Exemption (IDE) from the FDA is not required.

F. VERTEBRATE ANIMALS

Not applicable.

G. CONSULTANTS

An Advisory Board for the project will provide advice and guidance on clinical issues, engineering, and product development. The Advisory Board will also approve the Design Requirements. The Advisory Board chair will be Dr. Vaughn Adams and the membership is:

- Dr. Christina Kwasnica, the clinical co-investigator on this project. Dr. Kwasnica's experience and research interests are shown elsewhere in this proposal.

- Dr. Jiping He, an Associate Professor of Bioengineering at Arizona State University. Dr. He is Director of the National Science Foundation Neuromuscular Control Laboratory at ASU and has extensive experience with neuromuscular stimulation and control. He will consult on neurostimulation and EMG sensing and control issues.
- Deborah Koeneman has an MS degree in Bioengineering from ASU. She has worked for the Food and Drug Administration in regulation of Medical Devices. She currently is Director of Regulatory Affairs for OrthoLogic Corporation. She will consult on clinical trial, regulatory, and quality assurance issues.
- Glen Stranton, a manufacturing consultant in Phoenix, will consult on manufacturability issues. Glen has over 17 years experience managing manufacturing operations, many of them involving medical devices.
- Don Herring, an Assistant Professor of Industrial Design at ASU, will consult on human factors, industrial design, and attachment design.
- John Koeneman has a Bachelors Degree from MIT and an MBA from Harvard Business School. He recently retired from the investment banking firm he founded. He will consult on methods of achieving Phase III goals.

H. CONTRACTUAL ARRANGEMENTS

Not applicable for Phase I.

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29. M. Glanz , S. Klawansky, W. Stason, C. Berkey, T. Chalmers, "Functional Electrostimulation in Poststroke Rehabilitation: A Meta-analysis of the Randomized controlled Trials," Archives of Physical Medicine and Rehabilitation, 1996, Vol.77, pp.549-553.
30. J.D. Moreland, M. Thomson, A.R. Fuoco, "Electromyographic Biofeedback to Improve Lower Extremity Function After Stroke: A Meta-Analysis," Arch Phys Med Rehabil, Vol. 79, Feb. 1998, pp. 134-140.
31. S.L. Wolf, D.E. Lecraw, L.A. Barton, B.B. Jann, "Forced Use of Hemiplegic Upper Extremities to Reverse the Effect of Learned Nonuse Among Chronic Stroke and Head-Injured Patients," Experimental Neurology, Vol. 104, 1989, pp. 125-132.
32. E. Taub, N.E. Miller, T.A. Novack, E.W. Cook, W.C. Fleming, C.S. Nepomuceno, J.S. Connell, J.E. Crago, "Technique to Improve Chronic Motor Deficit After Stroke," Arch Phys Med Rehabil, Vol. 74, April 1993, pp. 347-354.
33. http://www.shadow.org.uk
34. J. Chae, R. Hart, "Comparison of Discomfort Associated with Surface and Percutaneous Intramuscular Electrical Stimulation for Persons with Chronic Hemiplegia," Am J Phys Med Rehabil, Nov/Dec 1998, Vol. 77, No. 6, pp. 516-22.

Principal Investigator *(Last, first, middle)*: Koeneman, James Bryant

Checklist

TYPE OF APPLICATION *(Check appropriate box[es].)*

[X] NEW application. *(This application is being submitted to the Public Health Service for the first time.)*

[ ] REVISION of previously-submitted application number ______
(This application replaces a prior unfunded version of a new application.)

[ ] CHANGE of Principal Investigator *(if applicable)*
Name of former Principal Investigator ______

1. ASSURANCES/CERTIFICATIONS

The assurances/certifications set forth below are made and verified by the signature of the OFFICIAL SIGNING FOR APPLICANT ORGANIZATION (small business concern) on the FACE PAGE of the application. Descriptions of individual assurances/certifications are found in application instructions under "Checklist." If unable to certify compliance with any item, provide an explanation and place it after this page.

• Human Subjects; • Vertebrate Animals; • Debarment and Suspension; • Drug-Free Workplace; • Delinquent Federal Debt; • Research Misconduct; • Civil Rights (Form HHS 690); • Handicapped Individuals (Form HHS 690); • Age Discrimination (Form HHS 690).

2. PROGRAM INCOME *(See discussion in application instructions under "Checklist.")*

All applications must indicate *(Yes or No)* whether program income is anticipated during the period for which grant support is requested.

[X] No [ ] Yes *(If "Yes," use the format below to reflect the amount and source(s) of anticipated program income.)*

Budget Period	Anticipated Amount	Source(s)

3. INDIRECT COSTS *(See discussion in application instructions under "Checklist.")*

Insert the rate, if known. If the applicant organization does not have a currently negotiated rate with the Department of Health and Human Services (DHHS) or another Federal agency, it must estimate the amount of indirect costs allocable (applicable) to the proposed Phase I project. That amount should be inserted in the space provided below. The applicant organization should also be prepared to furnish financial documentation to support the estimated amount, if requested by the Public Health Service. An applicant organization may elect to waive indirect costs if it so desires.

[ ] DHHS agreement, dated: ______ . ______ % salary and wages or ______ % Total Direct Costs.

[ ] No DHHS agreement, but rate established with ______, dated: ______

[ ] Rate negotiation pending with the National Institutes of Health.

[X] Indirect costs allocable (applicable) to this Phase I project are estimated to be $ 10,000

[ ] No indirect costs requested.

4. SMOKE-FREE WORKPLACE

Does your organization currently provide a smoke-free workplace and/or promote the non-use of tobacco products or have plans to do so?
[X] Yes [ ] No *(The response to this question has no impact on the review or funding of this application.)*

ARIZONA STATE UNIVERSITY

IGERT
INTEGRATIVE GRADUATE EDUCATION AND RESEARCH TRAINING

MAIN CAMPUS
PO BOX 879709
TEMPE, AZ 85287-9709

(480) 965-8034
FACSIMILE
(480) 965-4292

NEURAL AND MUSCULOSKELETAL ADAPTIONS IN FORM AND FUNCTION

BIOENGINEERING
BIOLOGY
EXERCISE SCIENCE
PHYSICAL ANTHROPOLOGY

March 27, 2001

Dear Dr. Koeneman,

The proposed project is exciting and the final product will be a valuable addition to the needed rehabilitation devices to help neurologically disadvantaged individuals regain motor function.

I am very glad to have this opportunity to work with you and your staff, as well as other experts, to develop a new system for motor disorder rehabilitation. I have been working on rehabilitation related research and teaching for the last ten years. Through the years I have accumulated expertise on neuromuscular control of posture and movement, spasticity evaluation and treatment, various neurological disorders such as multiple sclerosis, stroke, cerebral palsy, spinal cord injury, and Parkinson's disease, EMG recording and analysis, electrical stimulation, pneumatic muscles, and related instrumentation design and usage. I believe my knowledge can contribute significantly to the development of the system proposed in the application.

I would be happy to serve as a consultant in the Advisory Board. Please do not hesitate to let me know if you need any additional information.

Sincerely,

Jiping He, Ph.D.
Associate professor of Bioengineering
Director, IGERT Program on Neural & Musculoskeletal Adaptation in Form & Function
Department of Bioengineering
Arizona State University
Tempe, AZ 85287
(480) 965-0092
hjp@asu.edu

Exhibit B

Form Approved Through 05/2004
OMB No. 0925-0001

Department of Health and Human Services
Public Health Services

Grant Application

Follow instructions carefully.
Do not exceed 56-character length restrictions, including spaces.

LEAVE BLANK—FOR PHS USE ONLY.		
Type	Activity	Number
Review Group		Formerly
Council/Board (Month, Year)		Date Received

1. TITLE OF PROJECT
Development of a Massed Practice Stroke Therapy Device

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION ☒ NO ☐ YES
(If "Yes," state number and title)
Number: Title:

3. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR — New Investigator ☒ No ☐ Yes

3a. NAME *(Last, first, middle)*
Koeneman, James, Bryant

3b. DEGREE(S)
BSME MS PhD

3c. POSITION TITLE
President

3d. MAILING ADDRESS *(Street, city, state, zip code)*
1949 East Broadway Road
Tempe, AZ 85282

3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT

3f. MAJOR SUBDIVISION

3g. TELEPHONE AND FAX *(Area code, number and extension)*
TEL: (480)557-0448 FAX: (480) 557-0449

E-MAIL ADDRESS:
jbk@btic.com

4. HUMAN SUBJECTS RESEARCH ☐ No ☒ Yes

4a. Research Exempt ☒ No ☐ Yes
If "Yes," Exemption No. ______

4b. Human Subjects Assurance No.
None

4c. NIH-defined Phase III Clinical Trial ☒ No ☐ Yes

5. VERTEBRATE ANIMALS ☒ No ☐ Yes

5a. If "Yes," IACUC approval Date

5b. Animal welfare assurance no

6. DATES OF PROPOSED PERIOD OF SUPPORT *(month, day, year—MM/DD/YY)*		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT	
From	Through	7a. Direct Costs ($)	7b. Total Costs ($)	8a. Direct Costs ($)	8b. Total Costs ($)
07/15/02	01/15/03	$100,000	$100,000	$100,000	$100,000

9. APPLICANT ORGANIZATION
Name Kinetic Muscles, Inc.
Address 1949 East Broadway Road
Tempe, AZ 85282

Institutional Profile File Number (if known)

10. TYPE OF ORGANIZATION
Public: → ☐ Federal ☐ State ☐ Local
Private: → ☐ Private Nonprofit
For-profit: → ☐ General ☒ Small Business
☐ Woman-owned ☐ Socially and Economically Disadvantaged

11. ENTITY IDENTIFICATION NUMBER
EIN 86-1031432
DUNS NO. *(if available)*

Congressional District 1

12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE
Name Jame B. Koeneman
Title President
Address 1949 East Broadway Road
Tempe, AZ 85282

Tel (480) 557-0448 FAX (480) 55-0449
E-Mail jbk@btic.com

13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Name James B. Koeneman
Title President
Address 1949 East Broadway Road
Tempe, AZ 85282

Tel (480) 557-0448 FAX (480) 557-0449
E-Mail jbk@btic.com

14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

SIGNATURE OF PI/PD NAMED IN 3a.
(In ink. "Per" signature not acceptable.)
James B Koeneman

DATE
11/30/01

15. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF OFFICIAL NAMED IN 13.
(In ink. "Per" signature not acceptable.)
James B Koeneman

DATE
11/30/01

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. DO NOT EXCEED THE SPACE PROVIDED.

Stroke (CVA) is the leading cause of disability in the United States and it is estimated that its prevalence will more than double over the next 50 years. Current stroke therapy is labor-intensive and costly. The United States spends $17 billion taking care of stroke survivors. Recently, concentrated, massed practice therapies have been developed that improve function in CVA patients by reversing the effects of "learned nonuse". The objective of this project is to investigate the feasibility of a device that facilitates the administration of massed practice stroke therapy. The long-term objective is to provide a lightweight device for home use that provides motion and biofeedback of desired and undesireable muscle activity. Software controls the function of the device and monitors patient progress and compliance. A pneumatic artificial muscle will be used to provide physical motion. This artificial muscle has many of the properties of human muscle. It is lightweight, flexible and has spring like properties. This project will focus on treating wrist extensor weakness, however, the concept applies to all areas affected by motor impairment.

PERFORMANCE SITE(S) *(organization, city, state)*

Kinetic Muscles, Inc. Tempe, AZ
Barrow Neurological Institute at St. Joeseph's Hospital and Medical Center, Phoenix, AZ

KEY PERSONNEL. See instructions. *Use continuation pages as needed* to provide the required information in the format shown below.
Start with Principal Investigator. List all other key personnel in alphabetical order, last name first.

Name	Organization	Role on Project
Koeneman, James B.	Kinetic Muscles, Inc.	P.I.
Eblen, Cristobel	Southwest Behavioral Health Center	Statistical Consultant
Herring, Donald	Arizona State University	Human Factors, Indus Des.
Koeneman, Edward	Kinestic Muscles, Inc.	Device design & fabrication
Kwasnica, Christina	Barrows Neurological Institue	Physician evaluation
Wendelboe, Douglas	Kinetic Muscles, Inc.	Software & firmware design
Wolf, Steven	Emory University	Therapy concultant

Disclosure Permission Statement. Applicable to SBIR/STTR Only. See instructions. ☒ **Yes** ☐ **No**

The name of the principal investigator/program director must be provided at the top of each printed page and each continuation page.
Type density and size must conform to limits and specifications provided in the PHS 398 Instructions.

RESEARCH GRANT

TABLE OF CONTENTS

Page Numbers

* SBIR/STTR Phase I applications: Items A-D of the Research Plan are limited to 15 pages.

Appendix *(Five collated sets. No page numbering necessary for Appendix.)*

Appendices NOT PERMITTED for Phase I SBIR/STTR unless specifically solicited.

☐ Check if Appendix is Included

Number of publications and manuscripts accepted for publication *(not to exceed 10)* ______

Other items (list):

BUDGET JUSTIFICATION PAGE MODULAR RESEARCH GRANT APPLICATION				
Initial Budget Period	Second Year of Support	Third Year of Support	Fourth Year of Support	Fifth Year of Support
$ 100,000.00	$	$	$	$
Total Direct Costs Requested for Entire Project Period				$ 100,000.00

Personnel

During the 6 months of this project, the P.I. will have 30% effort. He will coordinate activities, manage the budget and provide biomechanical analysis. Edward Koeneman will have 30% effort during the 6 months. He will be responsible for hardware design, test and assembly of the devices to be used in the pilot study. Douglas Wendelboe will have 30% effort during the 6 months of the project and will be responsible for programming and data retrieval.

Consortium

Dr. Kwasnica's clinical practice will coordinate the patient recruitment and patient evaluation. The estimated costs are $13,500. The clinical measurements in the Barrow Neurological Clinic at St. Joseph's Medical Center are estimated to cost $12,500. The statistical consulting of Dr. Eblen plus the Human Factors consulting of Donald Herring plus the neuro rehabilitation theory consulting of Dr. He are estimated to be $3,300. Dr. Steven Wolf from Emory University will consult on concentrated practice, therapy protocols, and evaluation of results at no cost to the grant.

Fixed Fee (SBIR/STTR Only)
None

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
James B. Koeneman	Senior Biomechanics Consultant

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Minnesota, Minneapolis, MN	BSME	1959	Mechanical Engineering
Case Western Reserve University, Clevcland, OH	MS	1966	Bioengineering
Case Western Reserve University, Cleveland, OH	PhD	1970	Structures/Mechanical Design

RESEARCH AND PROFESSIONAL EXPERIENCE

1994 - present	Senior Bioengineering Consultant, BTI Consultants, Tempe, AZ. Assistive Devices, Biomechanics, Development of Composite Materials, Stress Analysis, Failure Analysis.
1994 - 1998	V.P. of Engineering, Orthologic Corporation, Tempe, AZ. Fracture fixation devices, bone growth stimulators.
1984 - 1994	Head of Bioengineering Division, Harrington Arthritis Research Center, Phoenix, AZ. Development of assistive devices, orthopedic implant design and testing, finite element analyses.
1981 - 1983	President, Paulson Medical Devices, Inc., Erie, PA. Development of fracture fixation devices and orthopedic implants.
1974 - 1981	Head of Bioengineering Division, Lord Corporation, Erie, PA. Development and manufacture of orthopedic implants. Composite material development.
1970 - 1974	Bell Telephone Laboratories, Columbus, OH. Development of Piezoelectric switching devices.
1960 - 1964	Reactor Engineer, U.S. Atomic Energy Commission, Argonne, IL.
1959 - 1960	Reactor Engineer, Argonne National Laboratory, Idaho Falls, ID.

PUBLICATIONS

Recipient of 16 patents, co-author of 22 publications and over 115 presentations at technical society meetings. Seven relevant publications listed below:

J.B. Koeneman and J.S. Kaiser, "A Functional Evaluation of the DataHand® Key Entry System User Experience Evaluated By Questionnaire," RESNA, 1994.

J.B. Koeneman and C. Eblen, "A Longitudinal Evaluation of Four-Wheeled Walker: Effects of Experience," Topics in Geriatric Rehabilitation, 8(3)3, 1993.

J.B. Koeneman, "Advanced Materials for Assistive Devices," Topics in Geriatric Rehabilitation, Vol. 8, No. 2, December 1992.

J.B. Koeneman, with others, "A Multi-Dimensional Evaluation of a Four-Wheeled Walker," Assistive Technology, Vol. 4, No. 1, 1992.

J.B. Koeneman, N. Reich, P. Otten, and J. Kaiser, "Clothing for Special Needs; An Information Arena," 10th Annual RESNA Conference, San Jose, CA, 1987.

J.B. Koeneman and M. Phillips, "Composite Materials for Rehabilitation Devices," 10th Annual RESNA Conference, San Jose, CA, 1987.

J.B. Koeneman, "State of the Art of Finite Element Analysis in Orthopaedics," Materials Research Society, Proceedings of Medical Devices and Materials Symposium, 1987.

AWARDS

International Fellow of Biomaterials Science and Engineering; International Union of Societies for Biomaterials Science and Engineering (1999)

Clemson Award for Contributions to the Literature, Society for Biomaterials (1997)

Fellow of Society for Advancement of Material and Process Engineering International (SAMPE) (1992)

Chapter Fellow Award, Society for Advancement of Materials and Process Engineering (SAMPE) (1990)

Engineer of the Year Award, Erie Engineering Society Council (1982)

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.
Photocopy this page or follow this format for each person.

NAME	POSITION TITLE
Steven L. Wolf, Ph.D., FAPTA	Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE (*if applicable*)	YEAR(s)	FIELD OF STUDY
Clark University, Worcester, MA	BA	1965	Biology
Boston University, Boston, MA	MS	1969	Physical Therapy
Emory University, Atlanta, GA	MS	1972	Anatomy
Emory University, Atlanta, GA	PhD	1973	Anat/Neurophysiology
Karolinska Institute, Stockholm, Sweden	Postdoctoral	1973-75	Neurophysiology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. **DO NOT EXCEED TWO PAGES.**

RESEARCH AND PROFESSIONAL EXPERIENCE

1969-70	Instructor, Anatomy and Physiology, Boston University, Boston, MA
1975-88	Principal Investigator, Emory University Rehab. Research & Training Center, Atlanta, GA
1975	Assistant Professor, Dept. of Surgery, Emory University School of Medicine, Atlanta, GA
1975-85	Assistant Professor, Dept. Anatomy, Emory University School of Medicine, Atlanta, GA
1975-78	Assistant Professor, Dept. of Rehab. Med., Emory University School of Medicine, Atlanta, GA
1978-85	Associate Professor, Dept. of Rehab. Med., Emory University School of Medicine, Atlanta, GA
1985-Present	Professor, Dept. of Rehabilitation Medicine, Emory University School of Medicine, Atlanta, GA
1988-2000	Director of Research, Dept. of Rehab. Med., Emory University School of Medicine, Atlanta, GA

HONORS

Marian Williams Research Award, 1980
Georgia Merit Award, Physical Therapy Association of Georgia, 1983
Golden Pen Award, American Physical Therapy Association, 1983
Catherine Worthingham Fellow of the American Physical Therapy Association, 1987
Outstanding Research Contributor to Advancing the Understanding of Biofeedback Mechanisms, Association of Applied Psychophysiology and Biofeedback, 1987
President, Association of Applied Psychophysiology and Biofeedback, 1991-92
Helen J. Hislop Award for Outstanding Contributions to Professional Literature, American Physical Therapy Association, 1993
Award of Excellence, Section on Clinical Electrophysiology, American Physical Therapy Association, 1993
Steven J. Rose Memorial Lectureship, Washington University, St. Louis, Missouri, 1994
Lucy Blair Service Award, American Physical Therapy Association, 1996
First John V. Basmajian Lectureship, International Society of Electrophysiology and Kinesiology, 1996
Section on Geriatrics, APTA, Outstanding published paper award, 1997.
Neurology Section, APTA, Outstanding Researcher Award, 1998.

Dr. Steve Wolf Appreciation Day, February 11, 1998, Warner-Robbins, Georgia: Outstanding Contributions to Rehabilitation in Georgia.
Lester Duplechen Outstanding Faculty Teacher Award, Department of Rehabilitation Medicine, 1999.
Stroke Council, American Heart Association, 1999.
APTA Mary McMillan Lecturer, 2002

SELECTED RELEVANT PUBLICATIONS (from over 200)

Wolf SL, Catlin PA, Ellis M, et al: Assessing the Wolf motor function test as an outcome measure for research with patients post-stroke. Stroke, 2001, in print.

Sathian K, Greenspan A, Wolf SL: Doing it with mirrors - a novel approach to stroke rehabilitation. J. Neural Repair and Neuroscience,14:73-76, 2000.

Wolf SL, Catlin PA, Ellis M, Link A, Morgan B, Piacentino A: Assessing the Wolf motor function test as an outcome measure for research with patients post-stroke. Stroke, 2000, submitted for publication.

Baer HR, Wolf SL: The modified Emory Functional Ambulation Profile: An outcome measure for the rehabilitation of post-stroke gait dysfunction. Stroke, 32:973-979,2000.

Kressig RW, Wolf SL, Sattin RW, O'Grady M, Greenspan A, Curns A, Kutner M: Associations between demographic and functional characteristics to activity-related fear of falling among older adults transitioning to fraily. J Amer Geriatr Soc, 2001, in print.

Griffith, JS Kreutzer, B Pentland (eds), Rehabilitation of the Adult and Child with Traumatic Brain Injury, third edition, FA Davis, Philadelphia, 2000.

Blanton S, Wolf SL: Effectiveness of upper extremity constraint-induced movement therapy on a patient with sub-acute stroke. Physical Therapy, 79:847-853, 1999.

Wolf SL, Catlin PA, Bonner B, Marks M, Weston M: Up-training loading responses in older adults. Applied Psychophysiology and Biofeedback, 24: 179-195, 1999.

Blanton S, Porter L, Smith D, Wolf SL: Strategies to enhance mobility in traumatic brain injured patients. In M. Rosenthal, ER

Wolf SL, Gregor RJ: Exploring unique applications of kinetic analyses to movement in older adults. J. Applied Biomechanics, 15:75-83, 1999.

Blanton SR, Wolf, SL: Effects of constraint-induced movement therapy intervention on individuals with upper extremity hemiparesis. Neurology Report, 1998, 22:164.

Taub E, Wolf SL: Constraint induction techniques to facilitate upper extremity use in stroke patients. Topics in Stroke Rehabilitation, 4:38-61, 1997.

Edgerton VR, Wolf SL, Levendowski DJ: Theoretical basis for patterning EMG amplitudes to assess muscle dysfunction. Medicine and Science Sports and Exercise, 28:744-751, 1996.

Edgerton VR, Wolf SL, Levendowski DJ, Roy RR: Evaluating patterns of EMG amplitudes for trunk and neck mucles of patients and controls. International J. Rehabiltation and Health, 2:1-18, 1996.

Edgerton VR, Wolf SL, Levendowski DJ: Theoretical basis for patterning EMG amplitudes to assess muscle dysfunction. Medicine and Science Sports and Exercise, 28:744-751, 1996.

Wolf SL, Segal RL, Catlin PA, Kantos H, Pate P, Raleigh T, Tschorn J: Determining consistency of elbow joint threshold angle in spastic elbow flexor muscles. Phys. Ther., 76:586-600, 1996.

Wolf SL, Segal RL: Downtraining human biceps-brachii spinal stretch reflexes. J. Neurophysiol., 75:1637-1645, 1996.

Wolf SL, Segal RL, Heter ND, Catlin PA: Contralateral and long latency effects of human biceps brachii stretch reflex conditioning. Exp. Brain Res., 107:96-102, 1995.

Wolf SL, Catlin PA, Blanton S, Edelman J, Lehrer N, Schroeder D. Overcoming limitations in elbow movement in the presence of antagonist hyperactivity. Phys. Ther., 74:35-44, 1994.

Wolf SL, Barton LA: Learned nonuse in the hemiplegic upper extremity. In Gordon WA (ed), Advances in Stroke Rehabilitation. Anover Medical Publishers: Boston, 1993, pp. 79-86.

Wolf SL, LeCraw DE, Barton LA, Jann BB: A comparison of motor copy and targeted feedback training techniques for restitution of upper extremity function among neurologic patients. Phys Ther, 69:719-735, 1989.

Wolf SL, LeCraw DE, Barton LA, Jann BB: Forced use of hemiplegic upper extremities to reverse the effect of learned non-use among chronic stroke and head injured patients. Exp Neurol, 104:125-132, 1989.
Evatt ML, Wolf SL, Segal RL: Modification of human spinal stretch reflexes: Preliminary studies. Neurosci Letters, 105:350-335, 1989.
Wolf SL, Binder-Macleod SA: EMG biofeedback applications to the hemiplegic patient: Changes in upper extremity neuromuscular and functional status. Phys Ther, 63:1393-1403, 1404-1413, 1983.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Christina M. Kwasnica M.D.	**Director of Brain Injury Rehabilitation**

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Arizona Tucson, AZ	BA	1991	Political Science
Northwestern University Medical School Chicago, IL	MD	1995	Medicine

POSITIONS:

Resident Physician Northwestern University Medical School/Rehabilitation Institute of Chicago Department of Physical Medicine and Rehabilitation Chicago, IL 1995-1999

Clinical Instructor and Cognitive Neurology Fellow Northwestern University Alzheimer's Disease Center Departments of Neurology and Physical Medicine and Rehabilitation Chicago, IL 1999-2000

Director of Brain Injury Rehabilitation Barrow Neurological Institute Phoenix AZ 2000-present

PROFESSIONAL AFFILIATIONS:

Diplomate, American Board of Physical Medicine and Rehabilitation

Fellow, American Association of Physical Medicine and Rehabilitation

Diplomate, Association of Academic Physiatrists

AWARDS AND HONORS:

Seabury Foundation Endowed Research Resident- July 1998-June 1999

NIH National Research Service Award Fellowship- F32 NS10858-01 August 1999-August 2000

Sara Baskin Award for Research Excellence- Rehabilitation Institute of Chicago- May, 1999

President's Citation- 62nd Annual Assembly of the American Academy of Physical Medicine and Rehabilitation- for outstanding paper presentation- "Predictors of Ambulation in Stroke Rehabilitation"

RESEARCH PROJECTS ONGOING OR COMPLETED DURING THE LAST THREE YEARS:

Current

Predictors of Ambulation in Stroke Rehabilitation with Dr. Richard Harvey, Rehabilitation Institute of Chicago

Pending

Unilateral Neglect and the Relationship of Measurements with Function

Prior

Bromocriptine in Unilateral Neglect- F32 NS10858-01
NIDRR Stroke Research and Training Center- Rehabilitation Institute of Chicago

PEER REVIEWED PUBLICATIONS:

Kwasnica, CM and Heinemann, A. "Coping with Traumatic Brain Injury: Representative Case Studies," Archives of Physical Medicine and Rehabilitation, April 1994, 384-389.

Grujic, Z, Mapstone, M, Gitelman, D, Weintraub, S, Johnson, N, Hays, A, Kwasnica, CM, Harvey, RL, and Mesulam, M. "Dopamine Agonists Reorient Visual Exploration Away from Neglected Hemisphere," Neurology, December 1998.

Kwasnica, CM. "Unilateral Neglect after Right Hemisphere Stroke- a Review of the Syndrome and Management," Critical Reviews in Physical Medicine and Rehabilitation, accepted for publication December, 2000.

SELECTED RECENT ABSTRACTS AND PRESENTATIONS:

Kwasnica, CM, Harvey, RL, and Mullarkey, C. "Predictors of Ambulation in Stroke Rehabilitation," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November, 2000

Kwasnica, CM, Cherney, L, and Harvey, RL. "Unilateral Neglect and Relationships with Functional Outcomes," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November, 1998.

Kwasnica, CM, Grujic, Z, Mapstone, M, and Harvey, RL. "Bromocriptine Effect on Unilateral Visual Neglect After Right Hemisphere Infarct: A Pilot Study," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November, 1997.

Managing Neglect Syndrome after Stroke: A Complete Experience- Annual Assembly of the American Academy of Physical Medicine and Rehabilitation, November, 1998.

Managing Neglect Syndrome after Stroke: A Complete Experience- Annual Multidisciplinary Stroke Course- Rehabilitation Institute of Chicago, April 1999

Pharmacology of Brain Injury- Rehabilitation Institute of Chicago- December 2000

Non-traumatic Brain Injury- Rehabilitation Institute of Chicago- December 2000

Pharmacologic Approaches to Motor Recovery after Stroke- Annual Multidisciplinary Stroke Course- Rehabilitation Institute of Chicago- April 2000

Atypical Dementias- Grand Rounds- Ingalls Hospital- Chicago, IL- April 2000

Neuroplasticity and Rehabilitation- Grand Rounds- Rehabilitation Institute of Chicago- July 2000

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Douglas E. Wendelboe	Software Consultant; President, Penn Microsystems

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Pennsylvania State University, State College, PA	BS	1972	Electrical Engineering
University of Pennsylvania, Philadelphia, PA	MS	1976	Electrical Engineering

RESEARCH AND PROFESSIONAL EXPERIENCE

1998-Present Software Consultant, BTI Consultants, Tempe, AZ. Design of hardware and software for medical devices

1981-Present President, Penn Microsystems. Consulting on microprocessor-based products. Medical device projects include:

- Hand-held Blood Prothrombin-Time Measuring Device, San Jose, CA, 2000-Present
- Designed and implemented the Automated Calibration and Test System for the Bone Growth Stimulator, Phoenix, AZ, 1999-2000
- Firmware enhancements for an electromagnetic Bone Growth Stimulator, Phoenix, AZ, 1997-1999
- Developed an Automated Active Burn-In System for the Bone Growth Stimulator, Phoenix, AZ, 1996-1997
- Designed and implemented firmware for Nerve Integrity Monitor Instrument, Jacksonville, FL, 1994-1995
- Designed, implemented, and maintained the firmware for a line of Micro-titer Plate Readers, Winooski, VT, 1982-1985
- Designed and implemented the complete firmware for a Pacemaker Systems Analyzer, Winooski, VT, 1980-1981

1977-1981 Senior Associate Engineer, IBM Corp., Essex Junction, VT

1976-1977 Senior Product Engineer, Honeywell Corp., Ft. Washington, PA

1972-1976 Design Verification Software Engineer, UNISYS (Sperry-Univac), Blue Bell, PA

PROFESSIONAL PUBLICATIONS

"Recommended Use of the PL/M Computer Language in Safety-Related Systems," Report for the Nuclear Regulatory Commission, NUREG/CR-6463, June 1996

Co-publisher of the Annual "Arizona High Tech Directory"

Columnist for the "Arizona High Tech Times" newspaper

PROFESSIONAL

IEEE Computers, IEEE Software, IEEE Management, IEEE Biomedical

American Society for Quality

TECHNICAL SKILLS

Languages: Keil C51 w/uVision2, IAR C, PIC-C, 8051, 8x86, 68xx, 68xxx assembler, Microchip PIC, Hitachi H8 assembler, TMS320C54x Algebraic assembler, National Instruments LabWindows/CVI, Microsoft Visual C++, Visual Basic

RTOS: uC/OS-II, QNX, Keil RTX-51, familiarity with VxWorks, Tornado

Microprocessors: Intel 8051, 80251, 8X93x USB, Intel 80x86, 80188, 386EX, 68HC05, 68HC08, 68HC11, 68xxx family, Hitachi 6303, H8S/2134, Microchip PIC16C74, 16C65, ST Micro ST10F167/168

In-Circuit Emulation: Intel ICE 8051, 8085, 80188, 80x86, Nohau EMUL51-PC: 80C552, 89C51RD2, Microchip PIC-Master & others

Peripheral Buses: I^2C, CAN v2.0, USB, Motorola SPI, Dallas Semiconductor interfaces

Design Standards: IS)-9001 Design Quality Standards, FDA (97-4179) Medical Device Quality Systems Standards, FDA 510(k), FDA Pre-Market Approval (PMA)

Bus Boards: PC/104 Bus, STD Bus, VME Bus

Logic: SPICE Simulation, Programmable Logic Compilers

Network: TCP/IP, WATTCP

Database: MS SQL7, Oracle, Informix

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Edward J. Koeneman	Consultant

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Arizona State University, Tempe, AZ	BSEET	1992	Electronic Engineering
Arizona State University, Tempe, AZ	MT	1994	Electronic Engineering

POSITIONS

1999-Present	BTI Consultants, Consultant.
1997-1999	Adtron Corp., Mesa, Arizona. Product Manager, Data Storage Devices.
1997	PCI Medical, Phoenix, Arizona. Design Engineer, Medical Electronics.
1995-1997	Prescom Electronics, Mesa, Arizona. Chief Engineer, Contract Electronic Design and Manufacturing.
1988-1995	Harrington Arthritis Research Center, Phoenix, Arizona. Lab Coordinator for Orthopaedic Resident Projects, Mechanical Testing.

PEER REVIEWED PUBLICATIONS

Koeneman, E.J., J.A. Lerman, R.J. Haynes, J.B. Koeneman, W. B. Wong, "A Biomechanical Comparison of Gardner-Wells Tongs and Halo Device Used for Cervical Spine Traction," SPINE, Volume 19, Number 21, pp. 2403-2406, 1994.

Koeneman, E.J., N.R. Crawford, A.G.U. Brantley, C.A. Dickman, "An Apparatus Applying Pure Nonconstraining Moments To Spine Segments In Vitro," *SPINE*, Volume 20, Number 19, pp. 2097-2100, 1995.

SELECTED PRESENTATIONS

Koeneman, E.J., J.A. Lerman, J.E. Maisel, J.B. Koeneman, "Electromyographic Analysis of the Hockey Slapshot," Presented at 1994 Fall Meeting of the Biomedical Engineering Society.

AWARDS AND HONORS

IEEE Outstanding Student Achievement Award, 1993

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Donald E. Herring	Senior Industrial Design Consultant

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
American University, Washington, DC	BA	1967	Govt. and Public Admin.
Arizona State University, Tempe, AZ	BS	1982	Product Design
Arizona State University, Tempe, AZ	MSD	1993	Human Factors and Design

PROFESSIONAL EXPERIENCE

2001-Present	Senior Industrial Design Consultant, BTI Consultants, Tempe, Arizona
1998-Present	Assistant Professor, Arizona State University, Tempe, Arizona
1997-1999	Proprietor, Redfish Design, Phoenix, Arizona
1994-1997	Assistant Professor, Purdue University, West Lafayette, Indiana
1992-1994	Exhibit and Industrial Designer, Sunbelt Scenic Studios, Inc., Tempe, Arizona
1991-1992	Exhibit Designer, Giltspur Exhibits, Phoenix, Arizona
1982-1989	Senior Project Designer, Mattel Toys, Hawthorne, California
1975	Arizona Real Estate Sales and Brokerage, Phoenix, Arizona
1973	Specialist, United States Treasury Department, Washington, D.C.
1972	Foreman, Athens Paint & Drywall Company, Alexandria, Virginia
1968	OJT Contract Writer, Washington Urban League, Washington, D.C.
1968	Capitol Policeman, United States Capitol Building, Washington, D.C.

PRINCIPAL PROFESSIONAL PUBLICATIONS AND PRESENTATIONS

"Children's Computer Human Factors and Seating Recommendations" (For Our Greatest Future Resource), Natural Resources, 1995 IDSA Design Education Conference Proceedings, Santa Fe, New Mexico, September 1995

"Twenty Years Later: What Are the 1 1982 Graduates of an Industrial Design Program Doing in the New Millennium?," Gumbo, 2000 IDSA Design Education Conference Proceedings, New Orleans, Louisiana, September 2000

MEMBERSHIPS IN SCIENTIFIC AND PROFESSIONAL SOCIETIES

Human Factors and Ergonomics Society of America
Arizona Chapter Member of the Human Factors and Ergonomics Society of America
Industrial Design Society of America (IDSA)
The Arizona IDSA Chapter Secretary (Founding member and officer)
The Indiana IDSA Chapter Secretary/Treasurer (Resigned, April, 1997)

PATENTS

U.S. Patent 4,787,876 - Toy Musical Play Set, 11/29/88, assigned
U.S. Patent 4,673,373 - Transformable Toy Block, 6/16/87, assigned
U.S. Patent 4,645,471 - Busy Ball Child's Toy, 3/7/85, assigned

AWARDS, SCHOLARSHIPS AND HONOR SOCIETIES

Netherlands Toy of the Year Award to Disney Pots and Pans Band based on Originality, Safety and Suitability, 1988

Second Place Award ($2,000.00) in Mattel's Toy of the Year Contest for the Invention and Development of the Double Dooz Transformers Toy Line, 1986

Nominated for the Mattel Toys Presidents Award for Leading a "Brainstorming Event" with 40 Participants Producing 100 Product Concepts for Presentation in Ten Days, 1985

Mattel $2000.00 Discretionary Award for "The First Innovative Preschool Product Line to Come out of Mattel in Eight Years," 1985
Arizona State University Outstanding Senior Industrial Design, 1982
Honorable Mention ($250.00) in Mattel Toy Design Contest, 1982
Awarded Internship at Mattel Toys, 1982
Phi Kappa Phi National Honor Society, 1982

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Cristobal Neal Eblen, Ph.D.	Director of Planning, Research and Program Evaluation

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Marist College	BA	1976	Psychology
Marist College	MA	1978	Community Psychology
Arizona State University	Ph.D.	1987	Social Psychology

NOTE: The Biographical Sketch may not exceed four pages. Items A and B may not exceed two of the four-page limit.

A. **Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

Post-doctoral Research Fellow (Harrington Arthritis Research Center) 1987-89
Psychologist I (AZ Department of Corrections) 1989-90
Psychologist II (Arizona State Hospital) 1990-91
Research and Statistical Analyst III (AZ Division of Behavioral Health Services) 1991-93
Psychologist II (Southern Arizona Mental Health Center) 1993-96
Psychologist II (AZ Department of Corrections) 1996-97
Research Associate (Community Partnership of Southern Arizona) 1997-2000

B. **Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation.

Eblen, C. & Koeneman, J. (1993). A longitudinal evaluation of a four-wheeled walker: Effects of experience. Topics in Geriatric Rehabilitation, 8, 65-72.

Eblen, C. (1992). Evaluation of assistive devices. Topics in Geriatric Rehabilitation, 8, 6-11.

Eblen, C. & Koeneman, J. (1991). A multi-dimensional evaluation of a four-wheeled walker. Assistive Technology, 3, 32-37.

C. **Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and responsibilities of principal investigator identified above.

N/A

RESOURCES

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

Laboratory:

KMI leases 1,433 square feet of office and laboratory space. Our lab contains the latest in hardware support tools such as: Logic analyzers, analog & digital oscilloscopes; I2C, USB and CAN bus analyzers; Internet server with TCP/IP tools. We also maintain the latest in software compilers, assemblers, simulators, and other software development tools for microprocessors and systems.

We have a complete model shop for the development of prototypes. This includes saws, sanders drill press and a complete supply of hand tools. We have a complete drafting facility.

These facilities are dedicated to the development of the device described in this proposal and to extensions of the design.

Clinical:

All clinical evaluations will be done at the Barrow Neurological Institute (BNI) of St. Joseph's Hospital in central Phoenix. It was first accredited by the Commission on Accreditation of Rehabilitation Facilities (CARF) in 1988. BNI has a state-of-the-art rehabilitation facility and participates in many clinical rehabilitation research studies. Space and equipment for the clinical evaluations will be available for this study.

Animal:

NA

Computer:

Various computer simulation programs such as AutoCAD, Photoshop, Ilustrator, Humanoid, Perception Video Capture Hunamoid run on eight Pentium computers.

Office:

The office has complete facsimile, copying and printing facilities.

Other:

The KMI facility is adjacent to BTI Consultants that provides secretarial and technician support and miscellaneous consulting on an as needed basis.

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of each.

See above.

INTRODUCTION

BTI Consultants submitted the original proposal. Because of clinical interest in this device, a separate company, Kinetic Muscles, Inc. (KMI) was formed in May 2001 and is now submitting this proposal. The PI and most of the participants are unchanged from the original proposal. Steven Wolf, Ph.D., PT, FAPTA, who is a clinician specializing in stroke rehabilitation and a well-respected research scientist in motor control is now a consultant. The scope of work for the original proposal involved fully developing the device per design control procedures. The work of Phase I has essentially been completed. Therefore, the Experimental Design has been completely rewritten to be a pilot clinical study, and because of this extensive rewrite, content changes are not indicated by change in font. The comments that follow are in sequential response to the concerns expressed by the reviewers on the summary statement of the original grant proposal. Their concerns are summarized, followed by our response. The responses are first lettered and the narrative page number where the total response can be found is given next.

Reviewer 1:

A. (pages 19-22) **Need for more detail on the design.** An overall block diagram of function is included and a more complete description included.

B. (pages 19,22,23,27) **What are the training parameters? How are issues of spasticity, ADLs, fatigue, etc. addressed?** A more thorough description of the treatment protocol is included in this revision and the resistance due to wrist and finger flexor spasticity is measured and fed back to the patient. The safety features of the patient being able to stop and start treatment at any time, the panic button, limit on force and range of motion are described in this revision. Activities of Daily Living (ADLs) are encouraged when the device is not being used.

C. (pages 19,24) **How will compliance be monitored? What about issues of durability, maintenance and robustness of the device?** The design description includes how compliance is recorded by the microprocessor. Maintenance and reliability will be evaluated by recording patient calls for assistance and by the final patient questionnaire.

D. (pages 19,27) **Define safety features.** The safety features are described in more detail.

E. (pages 23-25) **Define the evaluation procedure elements and when and how they are evaluated. How do project/development goals relate to ultimate feasibility?** To address the issue of feasibility, standard patient performance tests are included as is the determination of feasibility based on quantifiable improvements in function and patient compliance with the therapy protocol

F. (pages 6-8,13,23-26) **There is a need to relate design implementation and value to investigators background.** More detail on the protocol is included and the biodata sheets of Drs. Wolf and Eblen are added.

G. (pages 6-9,26,27) **There is a need for detail about subject/user characteristics.** In addition to the physiatrist, Dr. Kwasnica, we have added Dr. Wolf, an experience physical therapy researcher as a consultant, and Deborah Taylor, the physical therapist that will make all functional measurement. All of these clinicians have experience working with patients described in study entrance criteria.

H. (pages 6-9,23,24) **Lack of awareness between what the device will do and movement characteristics achieved.** Dr. Wolf has agreed to be an active consultant and correlations of physiological changes with functional changes included.

I. (pages 26,27) **Gender, minority or children issues must be discussed in great detail.** The patients expected to participate in the study are representative of those seen by physicians in this area.

Reviewer 2:

A. (pages19,20,22) **The device appears unwieldy.** The fully developed design described in this proposal has a battery driven micro-compressor that is very quiet and is lightweight. The patient perception of the unwieldiness will be evaluated in the Patient Acceptance Questionnaire. There is elastic recovery inherent in the driver.

B. **The evidence for utility of Functional Electrical Stimulation is questioned.** We agree that there are minimal results reported in the literature supporting the effectiveness of this treatment. To better evaluate the effectiveness of this treatment we have removed the neurostimulation component from the device in this study and will study it separately.

C. (pages 19,21,22) **More detail is needed for the EMG biofeedback function.** Diagrams of and descriptions of electrode placement and use in informing the patient of wrist extensor activity is described.

D. **Same as Comment E from reviewer 1.**

E. **What is meant by massed practice?** As discussed in the referenced literature, "massed practice" refers to repetitive practice in using the limb for many hours a day for a period of consecutive days.

F. **Same as Comments D. and I. from reviewer 1.**

Reviewer 3: This reviewer brought up the issues of lack of detail, feasibility assessment and more clinician involvement. These have all been discussed with respect to the other reviewers comments

RESEARCH PLAN

A. SPECIFIC AIMS

The **primary purpose** of this project is to improve the restoration of physical function of stroke patients by incorporating into one device, the treatment modalities of massed practice therapy, and force and electromyographic (EMG) biofeedback. Each of these approaches may in and of itself demonstrate varying degrees of success in treating stroke patients. The device will assist therapy by supplying increased amounts of information to the physician and therapist while reducing the amount of patient contact time. The device will be adaptable to accommodate the changing paradigm of CVA rehabilitation service delivery and to assist in studies designed to refine therapy protocols. The **hypothesis** to be tested is whether it is feasible for this biofeedback device to improve stroke patient physiological and functional performance. Using the wrist joint as a model, this approach will be deemed feasible if there is an increase in active range of wrist motion of 10% per week and there is a positive correlation between active wrist motion changes and changes in functional improvement as measured in the Wolf Motor Function Test (WMFT).

The **specific aims** of this proposal are:

1. Determine patient compliance to an extensive practice, at-home therapy protocol.
2. Measure the patient physiological changes of active range of wrist extension, EMG extensor activity, and flexor force resistance to motion during the course of therapy.
3. Ascertain patient functional changes over the course of therapy.
4. Analyze the relationship between functional changes and physiological changes.

B. BACKGROUND AND SIGNIFICANCE

Many people have movement disabilities caused by disease or injury. Among the causes are cerebrovascular accident or stroke (CVA), traumatic brain injury, multiple sclerosis, spinal cord injury and Parkinson's disease. This project focuses on stroke; however the results will have application to other causes of movement disability. Stroke is the leading cause of disability in the United States with at least 700,000 new cases each year [1-3]. Over half of these people have residual physical disability. Current stroke therapy is labor-intensive and costly. Often insurance does not cover the cost of full therapy. One estimate is that the United States spends $30 billion per year to take care of stroke survivors. Seventeen billion dollars of this cost is direct medical expenditures and thirteen billion dollars represent an indirect cost due to lost productivity [3]. Another estimate is that the total direct and indirect costs of stroke are $43.3 billion per year [3]. The number of strokes is projected to increase because of the increase in the over 50 "baby boom" population. Also, new pharmaceutical treatments for stroke are projected to increase the number of patients surviving a stroke and increase the percentage of stroke survivors requiring rehabilitation. Therefore, it is not surprising that a recent estimate indicates the prevalence of stroke will more than double over the next 50 years [2].

Because of health care reimbursement reductions, therapy time for stroke patients has been significantly decreased. Currently, a majority of time spent in therapy post-stroke concentrates on helping a patient adapt to their disability by teaching toileting skills and transfers. A consequence of this treatment is the emergence of "learned nonuse" that hinders the restoration of available function [2]. Most current rehabilitation therapies are administered on a spaced basis. Recently, concentrated therapies have been developed that improve function in CVA patients by reversing the effects of "learned nonuse"[4]. Animal studies suggest that learned nonuse is established immediately after the initial organic damage. A patient is punished for trying to use the affected limb and is rewarded for using other parts of the body. Over time, healing of the

organic damage occurs but the suppression of use learned in the acute phase remains in force [4]. As discussed by Taub [4], many of the therapies that have been shown to be effective in restoring function involve massed practice. Physical Therapy training techniques were used by Bach-y-Rita [5,6] and Franz, Scheetz, and Wilson [7]. Significant improvement in limb function was obtained in chronic CVA patients. Training techniques based on EMG biofeedback improved motor ability of chronic CVA patients, as demonstrated in studies by Wolf [8,9], Basmajian [10, 11], and Balliet [12]. Repetitive concentrated practice produced large therapeutic effects for lower limb function [13, 14, 15]. Taub (2,32) has systematically studied a variation of forced use of hemiplegic extremities, originally described by Wolf (31,35,36). Taub has labeled this therapy Constraint-Induced (CI) Movement Therapy [2, 32]. His group has shown positive results in controlled randomized studies [16]. Some of these experiments compared several massed therapy techniques and all showed very large increases in limb use over the treatment period.

Two very sophisticated robot systems are being developed for treatment and evaluation of CVA patients [1, 17]. These devices have shown some effectiveness in treatment of CVA patients and have developed very useful data for understanding recovery mechanisms; however, the current cost of these systems precludes their widespread clinical use [18].

Other studies show that measured EMG can be used to trigger neuromuscular electrical stimulation in restoring function to CVA patients [26, 27, 28, 29]. However, the discomfort of surface neuromuscular stimulation significantly limits the clinical implementation of this modality for persons with hemiplegia [34]. EMG biofeedback treatment of stroke patients has also shown some success [30, 31, 12, 8]. This treatment uses surface electrodes to capture the electrical activity of a selected muscle group. An electronic unit converts the signals into visual or audio information for the patient. This information is used by the patient to augment or decrease muscle activity.

A device that has a venerable history in supplying motion to assistive devices is the pneumatic artificial muscle. The artificial muscle exhibits many of the properties of human muscle. The device consists of an expandable internal bladder, e.g., a rubber tube, surrounded by a braided shell. When the internal bladder is pressurized, it expands radially against the braided shell. The pressure on the inside of the braid causes it to contract. Braided finger traps used to hold fingers on traction devices contract radially when pulled. The **air muscle** works in the same manner only in the opposite direction, i.e., increasing the diameter causes it to shorten. Like human muscle, the device has spring-like characteristics, is flexible, and is lightweight. The force-deflection characteristics can be made similar to those of human muscle. This type of device was first used in the 1950's for powered braces [19, 20]. Pressurized air canisters or accumulators that are recharged by air compressors supply air. Major advantages of the air muscle are its flexibility and ease of adaptation to address the specific loss of function exhibited by a patient. This type of device is often referred to as the McKibben Artificial Muscle. The device has three times the pull force of an air piston of the same cross sectional area. **The potential utility of this device resides in its unique combination of attributes: low cost, light-weight, low profile, and low noise operation.** The device has not been used extensively, because it has been applied in the wrong applications and has suffered from the lack of engineering in critical areas. Research on the application of the air muscle has been revived by the University of Washington [21, 22, 23, 24, 25]. The Shadow Organization in England uses the air muscle to operate biped and multiped robots [33].

C. PRELIMINARY STUDIES

The labor-intensive and long treatment times of forced practice make effective rehabilitation expensive. A promising approach to providing a lightweight, low-cost stroke therapy device is a system that synergistically combines four modes of feedback that individually have been shown to be effective (visual

presentation of desired motion, resistive-force of wrist flexor muscles and EMG activity of the extensor muscles). We have constructed a prototype of an air muscle powered therapy device for the hand and wrist that has the adaptability to be used in current treatment modalities and also in the refinement of rehabilitation methods. Figure 1 is a drawing of the device. An air muscle is attached to the proximal forearm. Activation of the air muscle rotates a bar that extends the wrist and operates a four-bar mechanism that extends the fingers. Wrist extension position is measured by a potentiometer that is incorporated in the device pivot. Resistance to extension is measured by force sensitive resistors (FSRs) placed on the driving bar. This is a measure of the combined wrist and finger flexor muscle resistance. Surface electrodes measure wrist extensor EMG activity. The location of the EMG electrodes is determined for each patient by the therapist. Figure 2 shows the method of permanently attaching the electrodes to the device. The method locates the electrodes on the same place on the patients arm for each therapy session. Air to activate the muscle is supplied by a microcompressor powered by a rechargeable 12-volt battery. A microprocessor controls the activation of the air muscle by operating the microcompressor and a 3-way valve. Wrist position is displayed as a bar graph on the LCD. The changing goal for active wrist motion is displayed as a line on the graph. One line of multi-color light emitting diodes (LEDs) indicates the degree of flexor resistance torque as measured by the force sensitive resistors. A second line of LEDs indicates the EMG activity of the wrist extensors. The microcompressor, battery, 3-way valve, microprocessor, and the LCD are in a plastic box that sits on a table during therapy sessions. The LEDs are arranged in lines on the plastic support structure on the arm. A coiled cable assembly that contains the electrical wires and air hose connects the box to the activation device. The batteries have the capacity to provide six hours of therapy a day and are recharged overnight. This system is a self-contained, mobile device that provides visual feedback of wrist and hand position, EMG wrist extensor activity and combined wrist and finger flexor resistive torque. The firmware in the microprocessor has been designed to be well-structured using object-oriented programming techniques. Use of these techniques yields more reliable code having fewer discrepancies and problems. Each of the object components was tested separately (component testing). When the firmware was integrated with the electronic hardware, the complete system was tested (system integration testing). Finally, the operation of the complete device was validated and verified for function by comparing to the design requirements established at the project beginning. The essence of the design requirements is described in this proposal. A block diagram of the system is shown in Figure 3. The real-time clock/calendar is powered by a battery mounted on the printed circuit board when the power is off. The clock maintains the time and date continuously. Records of patient use, active range of motion, extensor resistive torque, and EMG activity are recorded with a time stamp in a non-volatile serial EEPROM memory device. Data is kept safe, even when no power is applied to the memory. These records can be downloaded to a Windows application on the therapist's personal computer. The results are sorted by patient and tabular and graphical displays made available for viewing.

D. EXPERIMENTAL DESIGN AND METHODS

A pilot study will be conducted to determine the feasibility of this device to improve stroke patient physiological and functional performance.

Patient Population – The patient entrance criteria will be similar to the Extremity Constraint-Induced Training Evaluation (EXCITE) trial [37] except that patients must be more than 3 months post stroke with no limitation on the maximum time since their stroke. Patients must be at least 18 years old. A patient must be able to actively obtain more than 10° of wrist extension plus 10° of the thumb and at least two fingers 3 times in one minute. The patient must be able to independently and safely transfer to the toilet, stand-up and maintain balance for 2 minutes with arm support.

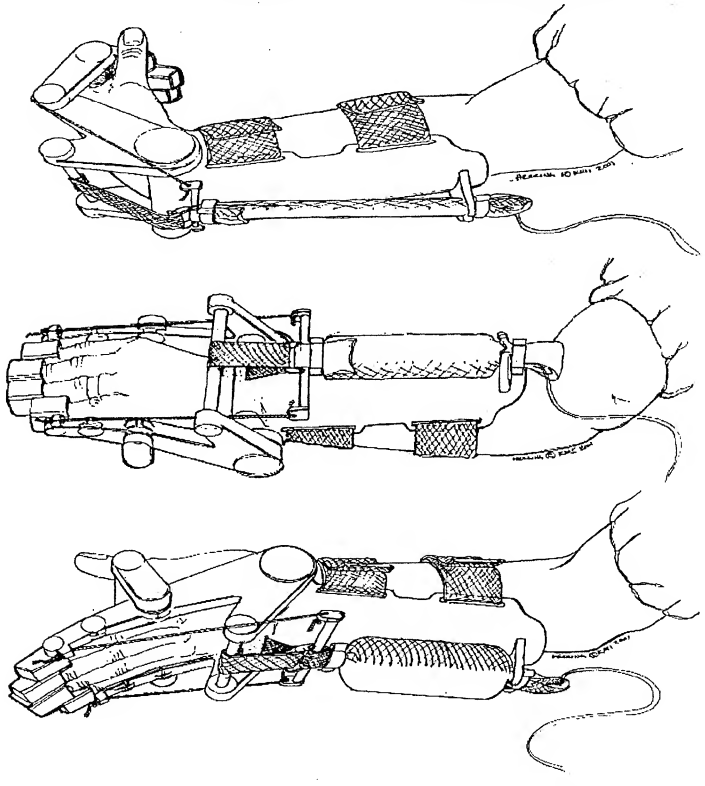


Figure 1 Therapy Device in Flexion, Neutral and Extension, Shrouding, LEDs and Control Box not shown for Clarity

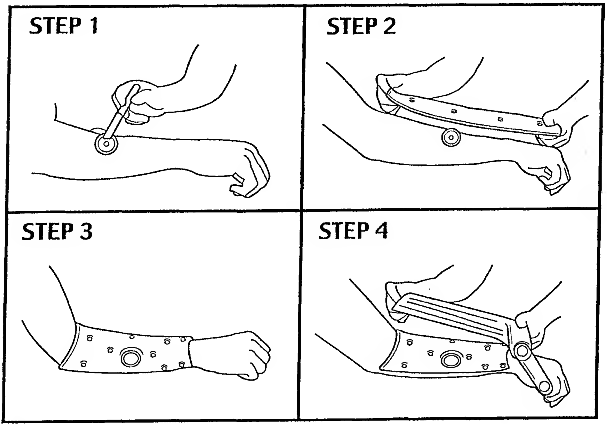


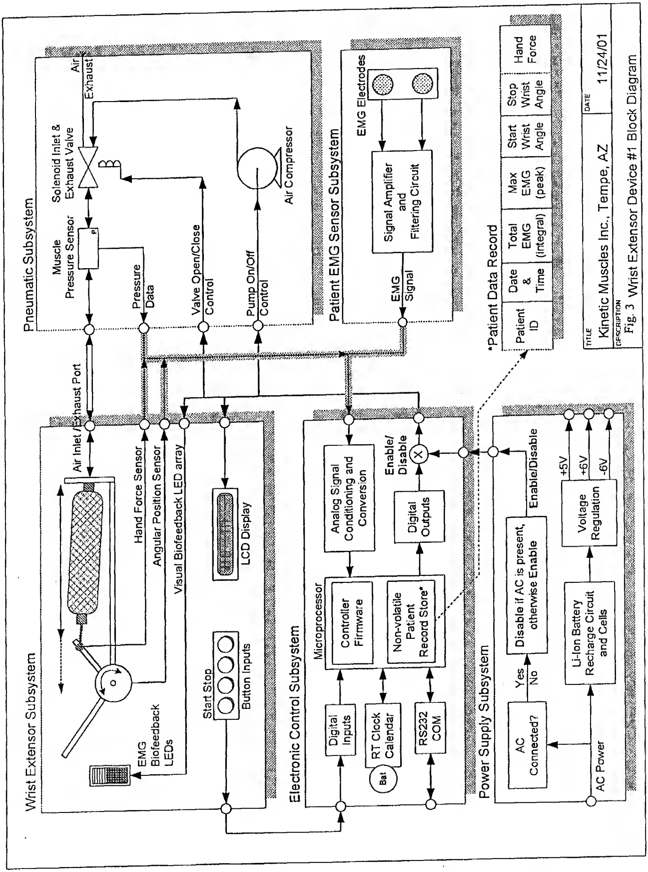
Figure 2 Attachment of EMG Electrodes.

Step 1: Therapist places electrodes so they measure wrist extensor activity. Transferable mark is placed on electrode.

Step 2: Carrier fabric is placed on arm. Hole is punched out for electrode.

Step 3: Carrier draped over arm around electrode.

Step 4: Plastic shell of device is placed over carrier and electrode. Adhesive on underside of shell adheres to carrier. Electrode is now part of shell and electrode is indexed with respect to palmar each time patient applies device.


Pneumatic Subsystem
Air Exhaust
Solenoid Inlet & Exhaust Valve
Muscle Pressure Sensor
Air Compressor
Pressure Data
Valve Open/Close Control
Pump On/Off Control
Patient EMG Sensor Subsystem
EMG Electrodes
Signal Amplifier and Filtering Circuit
EMG Signal
*Patient Data Record
Patient ID
Date & Time
Total EMG (integral)
Max EMG (peak)
Start Wrist Angle
Stop Wrist Angle
Hand Force
TITLE
Kinetic Muscles Inc., Tempe, AZ
DATE
11/24/01
DESCRIPTION
Fig. 3 Wrist Extensor Device #1 Block Diagram
Air Inlet / Exhaust Port
Hand Force Sensor
Angular Position Sensor
Visual Biofeedback LED array
LCD Display
Start Stop
Button Inputs
EMG Biofeedback LEDs
Wrist Extensor Subsystem
Analog Signal Conditioning and Conversion
Enable/ Disable
Digital Outputs
Microprocessor
Controller Firmware
Non-volatile Patient Record Store*
Digital Inputs
RT Clock Calendar
Bat
RS232 COM
Electronic Control Subsystem
Enable/Disable
+5V
+6V
-6V
Voltage Regulation
Disable if AC is present, otherwise Enable
Yes
No
AC Connected?
Li-Ion Battery Recharge Circuit and Cells
AC Power
Power Supply Subsystem

Patients are excluded from the study if they have had more than one stroke, have excessive cognitive impairments, lack of stamina, pain in the impaired extremity or serious, uncontrolled medical conditions.

The goal is for 15 patients complete the study. Because dropout rates of 10% to 24% have been reported in rehabilitation trials, we will recruit 25 patients. The three physicians involved with this study have already identified that many potential participants from their past or present patients.

Evaluation – Our physician colleagues will select patients whose medical records indicate that they meet the entrance criteria. The patients will be called into the clinic for an initial evaluation. After demonstrating and documenting that they meet the minimum requirements the patients will be asked to enter into a Behavioral Contract that expresses the investigators expectation that they comply with the protocol, that their participation is very important to improving therapy for stroke patients, and that the investigators are obligated to be responsive to questions and be available to the patients at reasonable times. The patient will be asked to sign the patient consent form.

Deborah Taylor, a registered occupational therapist who specializes in conducting clinical studies, will administer therapy. A patient history of age, type of stroke, date of stroke and previous treatments will be recorded. The therapist will document baseline patient wrist and hand performance as soon as the patient enters the study. The degree of true grasp reflex in response to palmar skin surface stimulation will be measured and recorded. The Wolf Motor Function Test (WMFT) [38] and the Frenchay Arm test [37] that have been validated in the literature will be used to assess function **[Specific Aim 3]**. The therapist will explain the operation and purpose of the device. A brochure describing the device and contact information will be provided the patient. The therapist will then place the EMG electrodes on the patient and attach them to the device. The therapist will demonstrate several treatments of the device. The device will be removed and the patient asked to attach the device and start treating without any help. The patient will be given a diary to record activities that he/she perform to attempt to manipulate the environment by the affected limb during the two weeks of the study. The patient will be instructed to attempt activities that they haven't done yet as function improves. The patient will be required to return after one week and at the end of two weeks for repeat functional evaluations. At the end of the study, the patient will be asked to fill out a questionnaire rating on an ordinal scale their impression of the device weight and bulkiness, their fatigue during therapy, the effectiveness of the LED and LCD feedback methods, the reliability of the device and they will be asked to provide suggestions.

Protocol – The patient is instructed to try to extend the wrist and fingers when a beep is heard. The EMG activity of the wrist extensors and the motion of the wrist **[Specific Aim 2]** are recorded in the memory of the device and displayed for the patient. The patient will be instructed to use the device for at least 6 hours a day, although more treatment is allowed. The treatments do not have to be continuous. The patient can start and stop the device at any time. The first 2 hours will emphasize EMG and joint position feedback. During the second 2 hours the flexor resistance torque from the flexors will be used as the feedback signal to help the patient reduce any flexor spasticity. The final 2 hours of therapy will have both extensor EMG and flexor resistance torque as feedback. The number of completed cycles will be recorded for each day as well as the time for each cycle and the total treatment time for each day. A 2 inch by 4 inch by 4 inch block is provided the patient. The patient is encouraged to grasp the block and lift it several times during a day and at the end of each therapy session. After grasping the patient is encouraged to try and lift and move the block. The patient is encouraged to keep a record of successful attempts.

The level of extensor EMG activity is indicated by LEDs. A level equal to that obtained at the last clinic therapy session shows a yellow light. A level below that level generates a buzzing sound. A green LED will indicate a higher level. Faster flashing LEDs will indicate higher levels of EMG activity. The output of the

joint position sensor is displayed on the LCD by a bar. If motion exceeds this line a pleasant sound is heard. After every day, the line that represents the goal is increased by 1% of the highest joint motion achieved in the previous day. Thus joint position serves as the basis for subsequent training each day.

During training, whenever motion has stopped for 3 seconds, the air muscle is activated and the wrist and finger extension is completed. The extension is held for 3 seconds and then released. The torque of the wrist and finger flexor resistance is measured and displayed on flashing red LEDs during the process. The higher the force, the faster the blinking. The patient will be instructed to try to minimize this force by thinking about relaxing the flexors. There is then a system delay of 10 seconds and the process started over with a beep.

The number of hours of operation of the device and the active motion achieved at the beginning of a day and at the end of each day is recorded in memory **[Specific Aim 1]**. This information will provide us with accurate information about patient compliance and allows us to match up our timed data from patient reports of self-documentation of training. When the device is turned on for the first time each day, these parameters are displayed for the patient on the LCD.

The memory of the device will be downloaded onto a PC in the clinic. A summary chart graphically displaying the number of hours of use a day by the patient, the range of motion change per day and the change of active range of motion day to day will be displayed and the charts printed for the patient file.

Data Analysis -
Measures: There are four types of data collected in this study:

(1) The *number of hours* of use per day by the patient. This is a measure of *compliance* with treatment and will be used to assess both functional improvements and study termination (i.e., dropout rate).

(2) The *physiological parameters* of wrist extensor EMG, wrist and finger flexor resistance torque, and active range of motion. *Range of motion* will be examined as a dependent variable, while resistance torque will be examined as both a dependent measure and a possible moderator factor influencing compliance and dropout rate.

(3) *Functional changes* in hand and wrist function are measured by standard test protocols at baseline, one week and at the end of the study. Attention will be made to assess those *functional assessments* in the protocol that should directly be impacted by this treatment; other assessments will be examined for generalization of functional improvement.

(4) *Patient activities and acceptance* of the device are recorded in self-report questionnaires. It is expected that self-reported acceptance and increase in activities will be related to compliance, physiological and functional gains.

Design and Statistics. The basic comparison is baseline with two time measurements (one week and post treatment). Specifically, physiological and functional changes will be examined using pre-post statistics. A Friedman test for repeated measures will be used to determine significant changes from baseline and post-test periods (baseline-one week comparisons will also be examined). To determine precise areas of change, follow-up Wilcoxon rank tests will be employed on individual measures.

Of specific interest will be the physiological range of motion assessment and those functional measures that are related to wrist functioning. This will help in reducing the multiple comparisons. The resistance torque will also be examined in this manner; however, correlational analyses will also be conducted to assess possible effects of spacticity as a moderator of success. Graphs plotting this relationship will be used to assess possible curvilinearity. **[Specific Aim 4]**

Given the small N in this study, there may be problems with the amount or quality of change variation to detect degree of improvement with initial disability. This analysis will be conducted. Correlation coefficients will be calculated between the physiological response changes (i.e., grasp reflex) and functional changes as well as reported changes in activities and compliance.

Finally, patient acceptance of the device and suggested improvements will be entered into the design control system for the device for evaluation. Correlations will be calculated between reported compliance and actual hours of use.

The device will be considered acceptable and feasible if patient compliance is sufficient to result in statistically valid improvements in both physiological function and functional measures. **[Hypothesis Test]**

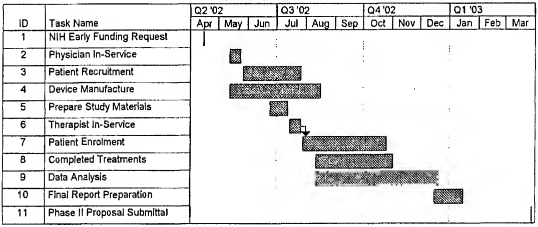
Limitations - By taking patients as early as 3 months post stroke, there may be some spontaneous recovery; however, it coincides with the lower limit of the EXCITE study. Also, Duncan has shown that the most dramatic motor recovery occurs in the firs 30 days following a stroke for all degrees of stroke severity [39]. We do not know if we are bringing sub-acute patients back to a pre-existing level or making absolute improvements. However, the study does measure the feasibility of usage and functional improvement. Because of the six-month limitation of a Phase I grant, follow-up to examine retention of gains or potential increased improvements with more therapy cannot be made. While the numbers of minority and ethnic people in this study preclude statistically significant comparisons, the main purposes of this study are to refine the protocol for a larger Phase II study and to investigate feasibility of this therapeutic device in a group of patients.

Design Issues – The sensitivity of the EMG measurement to forearm motion and relative motion of muscles with respect to skin will be examined. The repeatability of placement of the electrodes from use to use will also be evaluated. Skin sensitivity to the pressure of the device or type of material will be examined.

Project Plan - Table I is a time line (Gantt chart) of the Phase I tasks. Since six months is a brief time to conduct a pilot study, 90 days before the award of the study we will request NIH approval to accumulate costs before the beginning of the grant period. The early tasks would allow the patient portion of the study to begin immediately at the time of award. After NIH approval of early cost accumulation, the first task is to have an in-service for referring physicians to acquaint them with the theory behind the therapy protocol, the specific functioning of the device, and the patient entrance criteria for the study. At the same time, long lead-time parts for the study devices would be ordered, followed by assembly and device quality checks in task 4. Once the physicians are fully familiar with the device and the study, patients that are recommended by the participating physicians will be contacted in task 3. Patient information kits will be sent to them describing the purpose and protocol of the study. Follow-up phone calls will be made to answer any questions and ascertain their willingness to participate in the study and to schedule physician appointments for those that choose to participate. Just before beginning of the study, an extensive in-service session will be conducted for the therapist that will be conducting the patient evaluations and training. Task 6 is the preparation of study materials such as patient evaluation forms, individual patient study binders, and schedule charts. Task 7 is the therapy portion of the study. One patient a day will be scheduled with Dr.

Kwasnica on Monday, Wednesday, and Friday. Immediately following the physician evaluation, each patient will start the program under the direction of Deborah Taylor, OTR. In the second week of the study the therapist will see one starting patient and one follow-up patient on Monday, Wednesdays and Fridays. The therapist will see one start patient and two follow-up patients MWF on weeks 3, 4, 5, 7, and 8. In weeks 6 (Labor Day) and 9 (the final start week) the therapist will see six and eight patients respectively. In weeks 10 and 11 the final follow-up measurements will be made. Task 8 is the time period for completion of individual therapies. Upon completion of the protocol, the therapist will compile the downloaded data from the device and assemble all of the performance data and assign a confidential code number. Dr. Kwasnica and Ms. Taylor will review the study binder and provide it for data analysis. In task 9 the data will be analyzed as the patients are completed and a final summary prepared. This time line assures that all the 25 patients including prospective drop-outs can be recruited and accommodated in the 6 month time frame and this can only be done by us taking a proactive role to assure that all equipment and relevant supplies are gathered and in place before the official start date of the 6-month award. A final report addressing the feasibility of the device, device changes suggested by the results, and protocol changes suggested for the Phase II study. Assuming feasibility is demonstrated, an application for Phase II funding will be prepared for April 1, 2003, submission.

Table I Gantt Chart



E. HUMAN SUBJECTS

Involvement of Human Subjects: The purpose of the device under evaluation in this proposal is to facilitate the application of concentrated practice for stroke patients. Numerous studies, most notably by Taub and Wolf, have provided this therapy through one-on-one contact with physical therapists. In all of these studies there is no reason to believe that this intervention provides selective benefits (or limitations) based upon gender or racial attributes. In this study the gender and minority status will be recorded and reported for all patients. The patients identified by the participating physicians have the following demographics: 3 female and 4 male Hispanic or Latino; 7 female and 11 male not Hispanic or Latino; 1 male American Indian; 1 female and 3 male Black or African Americans; 9 female and 11 male of the White race. No Asian or Pacific Islanders were identified in the patient pool. The subjects of this pilot study roughly represent the population mixture of Maricopa County. The percentage of males in the study, 60%, is higher than the slightly less than 50% in the overall population. The study has 28% Hispanics compared to 24.5% in the population. The respective study and population percentages of the races are: Black or African American 16% versus 3.7%; Asian Native Hawaiian or other Pacific Islander 0% versus 2.3%; Native American 4% versus 2.0%. The small size and short time of this study make it difficult to exactly match the race, gender and ethnic background of the population. The numbers are so small that little meaningful statistical

conclusions can be made although physiological and functional performance will be reported for these categories. Children less than 18 years of age are excluded because an immature nervous system may respond differently to this therapy than a mature one and the low number of young patients available for this short study.

Human Research Material: All subjects will be individuals who have sustained a stroke 3 months prior to enrollment in this clinical trial. Subjects will be excluded if they do not meet our lowest level of minimal motor criteria and: 1) have a score of less than 24 on the Folstein Mini-Mental State Examination; 2) have sustained a stroke less than 3 months prior to the initiation of therapy; 3) are less than 18 years old (given an immature nervous system may respond differently to this type of therapy than a mature nervous system); 4) show a clinical judgment of excessive frailty or lack of stamina; 5) have serious uncontrolled medical conditions; 6) demonstrate excessive pain in any joint of the more affected extremity that could limit ability to cooperate with the intervention, as judged by the examining clinician; 7) have passive range of motion less than 45 degrees for: abduction, flexion or external rotation at shoulder, or pronation of forearm; or greater than 30 degrees flexion contracture at any finger joint (patients who pass the motor criteria specified above do not tend to have the type of pain or limitation of movement that would exclude them from treatment); 8) cannot stand independently for 2 min., transfer independently to and from the toilet or perform sit-to-stand;

Obtaining Past Data: All past data will be in the form of medical records and radiographic materials designed to confirm the diagnosis, site and type of lesion. These data will be obtained specifically for research purposes. The identity of patients and their medical records will be protected. Patient participants in this trial will receive codes to protect their identity throughout the study.

Recruitment of subjects: A majority of the patients will come from the practice of Dr. Kwasnica. Patients will also be recruited from Dr. Kwasnica's partners and from Rhodes Rehabilitation Hospital in Mesa (Dr. Kosak), and Boswell Medical Center in Sun City, AZ (Dr. Lachman). The patients will be referred to Dr. Kwasnica's facility for treatment. Dr. Kwasnica has identified 15 patients that meet the criteria. Dr. Kwasnica's partners, Drs. Kosak and Lachman have identified 5 each. Of these the physicians estimate that a total of 25 of these patients will participate in the study. All subjects will sign informed consents at the time of enrollment. These consent forms will be approved by the Institutional Review Board of St. Joseph's Medical Center. The information contained therein describes the study, its purpose and duration, appropriate contact personnel, risks and discomforts, benefits, etc.

Potential Risks: The physical risk involved with using this device is overextending a joint and causing soft tissue damage. Another risk is fatiguing the patient and causing anxiety. The risks involved with use of EMG electrodes are skin irritation. The only psychological risk might occur if a patient feels frustrated by their lack of progress. A control on this risk is that the patient has the right to drop out of the study at any time.

Minimization of Risk: The risk of overstretching a joint is controlled in several ways. There is a physical stop incorporated in the side bearing that prevents wrist extension over 60°degrees of extension. If the wrist is stopped by an obstruction, the force is limited by the low stiffness of the air muscle actuator. Also, if the torque measured by the extension bar exceeds 8 newton meters (the resistive torque of the finger and wrist flexors), the air is exhausted and the device shut down. A panic button is also provided for easy access by the unaffected hand that will also exhaust the air muscle and shut the device down if the patient is feeling any discomfort, fatigue or anxiety.

Reasonableness of Risk: As noted above, effective means of controlling the risks are designed into the device. When one realizes that the potential benefit can be substantially enhanced function in real world

activities and improved quality of life beyond that achieved during the early rehabilitation interval, the risks are not significant.

FDA Approval: It is our opinion that this device is not a significant risk device and that only IRB approval is required. We will submit the protocol, a description of the device, a patient consent form, and an evaluation of the hazards involved in use of the device and how we are controlling these hazards to the Barrow Neurological Institute/St. Joseph Medical Center IRB.

F. VERTEBRATE ANIMALS

Not applicable.

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H. CONTRACTUAL ARRANGEMENTS

Dr. Wolf is participating at no cost with the anticipation that this study will lead to a device that is supportive of the treatments being studied in the EXCITE trial.

The applicant organization and St. Joseph's Medical Center/ St. Joseph's Medical Center are prepared to establish in writing the required contractual agreements whereby the clinical institutions will provide physician and therapist services as described in this proposal. The cost of providing these services is included in the budget of this proposal. The applicant organization will pay the clinical institution charges based on an agreed upon per patient fee.

I. CONSULTANTS

An Advisory Board for the project will provide advice and guidance on clinical issues, engineering, and product development. The members of the Advisory Board are:

- Dr. Steven Wolf, Ph.D., Professor of Rehabilitation Medicine at Emory University. Dr. Wolf is the principal investigator of a randomized national clinical trial to explore the effect of forced use therapy on patients who have sustained a stroke. He will be advising on the treatment and evaluation protocols and provide general guidance on the treatment of stroke patients.
- Dr. Jiping He, an Associate Professor of Bioengineering at Arizona State University. Dr. He is Director of the NSF Neuromuscular Control Laboratory at ASU and has extensive experience with neuromuscular stimulation and control. He will consult on neurostimulation and EMG sensing and control issues.

- Deborah Koeneman has a MS degree in Bioengineering from ASU. She has worked for the Food and Drug Administration in regulation of Medical Devices. She currently is Director of Regulatory Affairs for OrthoLogic Corporation. She will consult on clinical trial, regulatory, and quality assurance issues.
- Don Herring, an Assistant Professor of Industrial Design at ASU, will consult on human factors, industrial design, and attachment design.
- Cristobel Eblen, Ph.D., Cris is a psychologist with experience in designing patient evaluation studies and questionnaires and performing statistical analyses.

CHECKLIST

TYPE OF APPLICATION *(Check all that apply.)*

☐ NEW application. *(This application is being submitted to the PHS for the first time.)*

☒ SBIR Phase I ☐ SBIR Phase II: SBIR Phase I Grant No. ______ ☐ SBIR Fast Track

☐ STTR Phase I ☐ STTR Phase II: STTR Phase I Grant No. ______ ☐ STTR Fast Track

☒ REVISION of application number: 1 R43 HD41805-01

(This application replaces a prior unfunded version of a new, competing continuation, or supplemental application.)

☐ COMPETING CONTINUATION of grant number: ______

(This application is to extend a funded grant beyond its current project period.)

☐ SUPPLEMENT to grant number: ______

(This application is for additional funds to supplement a currently funded grant.)

INVENTIONS AND PATENTS *(Competing continuation appl. and Phase II only)*

☐ No

☐ Yes. If "Yes," ☐ Previously reported ☐ Not previously reported

☐ CHANGE of principal investigator/program director.

Name of former principal investigator/program director: ______

☐ FOREIGN application or significant foreign component.

1. PROGRAM INCOME *(See Instructions.)*

All applications must indicate whether program income is anticipated during the period(s) for which grant support is request. If program income is anticipated, use the format below to reflect the amount and source(s).

Budget Period	Anticipated Amount	Source(s)
	0	

2. ASSURANCES/CERTIFICATIONS *(See instructions.)*

The following assurances/certifications are made and verified by the signature of the Official Signing for Applicant Organization on the Face Page of the application. Descriptions of individual assurances/certifications are provided in Section III. If unable to certify compliance, where applicable, provide an explanation and place it after this page.

•Human Subjects; •Research Using Human Pluripotent Stem Cells• •Research on Transplantation of Human Fetal Tissue •Women and Minority Inclusion Policy •Inclusion of Children Policy• Vertebrate Animals• •Debarment and Suspension; •Drug- Free Workplace *(applicable to new [Type 1] or revised [Type 1] applications only)*; •Lobbying; •Non-Delinquency on Federal Debt; •Research Misconduct; •Civil Rights (Form HHS 441 or HHS 690); •Handicapped Individuals (Form HHS 641 or HHS 690); •Sex Discrimination (Form HHS 639-A or HHS 690); •Age Discrimination (Form HHS 680 or HHS 690); •Recombinant DNA and Human Gene Transfer Research; •Financial Conflict of Interest (except Phase I SBIR/STTR) •STTR ONLY: Certification of Research Institution Participation.

3. FACILITIES AND ADMINSTRATIVE COSTS (F&A)/ INDIRECT COSTS. See specific instructions.

☐ DHHS Agreement dated: ______ ☒ No Facilities And Administrative Costs Requested.

☐ DHHS Agreement being negotiated with ______ Regional Office.

☐ No DHHS Agreement, but rate established with ______ Date ______

CALCULATION* *(The entire grant application, including the Checklist, will be reproduced and provided to peer reviewers as confidential information. Supplying the following information on F&A costs is optional for for-profit organizations.)*

a. Initial budget period:	Amount of base $ ______	x Rate applied ______	% = F&A costs	$ ______
b. 02 year	Amount of base $ ______	x Rate applied ______	% = F&A costs	$ ______
c. 03 year	Amount of base $ ______	x Rate applied ______	% = F&A costs	$ ______
d. 04 year	Amount of base $ ______	x Rate applied ______	% = F&A costs	$ ______
e. 05 year	Amount of base $ ______	x Rate applied ______	% = F&A costs	$ ______
			TOTAL F&A Costs $	

*Check appropriate box(es):

☐ Salary and wages base ☐ Modified total direct cost base ☐ Other base *(Explain)*

☐ Off-site, other special rate, or more than one rate involved *(Explain)*

Explanation *(Attach separate sheet, if necessary.)*:

4. SMOKE-FREE WORKPLACE ☒ Yes ☐ No *(The response to this question has no impact on the review or funding of this application.)*

EMORY UNIVERSITY SCHOOL OF MEDICINE
CENTER FOR REHABILITATION MEDICINE
1441 Clifton Road, N.E. Atlanta, Georgia 30322

DEPARTMENT OF REHABILITATION MEDICINE

(404) 712-5507

November 26, 2001

Mr. James B Koeneman, President
Kinetic Muscles, Inc.
1949 East Broadway Road
Suite D
Tempe, AZ 85282

Dear Jim:

I have read your revised SBIR proposal, "Development of a Massed Practice Stroke Therapy Device"(1 R43 HD41805-01) regarding the application of your combined force feedback and EMG biofeedback pneumatic muscle instrumentation to facilitate improved movement and function in the wrists and digits of patients who have sustained a stroke but in whom movement initiation into extension exists. The refinements in the device construct and in the implementation/analysis plan are excellent.

As you know, I have spent considerable time researching criteria for the use of EMG biofeedback applied to the upper extremities of patients after stroke. I have also done considerable work in the area of "forced use" or "constraint induced movement therapy" among stroke patients and currently am PI on the NIH funded EXCITE (EXtremity Constraint Induced Therapy Evaluation) national clinical trial. I will be more than honored to serve as a consultant to your project. As you know I am very concerned that the potential to use multi-modal (muscle and force) physiological feedback be made optimal and researched with extreme vigor. I believe that your device will assist in the delivery of excellent product development and well-performed research. I have met many of your staff and am acutely aware of their commitment to this project.

Good luck with your efforts. If I can assist in any way during the final preparation of this proposal, please feel free to call upon me.

Steven L. Wolf

STEVEN L. WOLF, Ph.D., FAPTA, PT
Professor, Department of Rehabilitation Medicine
Professor of Geriatrics, Department of Medicine
Associate Professor, Department of Cell Biology
Director, Program in Restorative Neurology (PROREN)
Emory University School of Medicine

Barrow Neurological Institute®
St. Joseph's Hospital and Medical Center

June 1, 2001

To whom it may concern:

This letter shall serve as a letter of support for the Small Business Innovation Research grant titled "Development of a Massed Practice Stroke Therapy Device." I am pleased to be asked to participate in the opportunity to engineer a device that may assist patients in applying the principles of massed practice in their stroke recovery.

As Director of Brain Injury Rehabilitation at Barrow Neurological Institute, I have the background to be able to participate in such research. I am looking forward to collaboration in this study.

Sincerely,
C. Kwasnica MD
Christina Kwasnica M.D.
Attending Physiatrist
Barrow Neurological Institute
St. Joseph's Hospital & Medical Center
Phoenix, AZ 85013

St. Joseph's Hospital
and Medical Center

350 W. Thomas Road
Phoenix, AZ 85013
(602) 406-3000 or 1-800-BARROW-1
http://www.chw.edu/bni

Exhibit C

Form Approved Through 05/2004
OMB No 0925-0001

Department of Health and Human Services Public Health Services **Grant Application** *Follow instructions carefully.* *Do not exceed 56-character length restrictions, including spaces.*	**LEAVE BLANK—FOR PHS USE ONLY.** Type / Activity / Number Review Group / Formerly Council/Board (Month, Year) / Date Received

1. TITLE OF PROJECT
Development of a Massed Practice Stroke Therapy Device

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION ☐ NO ☒ YES
(If "Yes," state number and title)
Number: PHS 2002-2 Title: SBIR

3. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR	**New Investigator** ☒ **No** ☐ **Yes**
3a. NAME *(Last, first, middle)* Koeneman, James, Bryant	3b. DEGREE(S) BSME MS PhD
3c. POSITION TITLE President	3d. MAILING ADDRESS *(Street, city, state, zip code)* 1949 East Broadway Road, Suite D Tempe, AZ 85282
3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT	
3f. MAJOR SUBDIVISION	
3g. TELEPHONE AND FAX *(Area code, number and extension)* TEL: (480)557-0448 FAX: (480) 557-0449	E-MAIL ADDRESS: jkoeneman@kineticmuscles.com
4. HUMAN SUBJECTS RESEARCH ☐ No ☒ Yes 4a. Research Exempt ☒ No ☐ Yes If "Yes," Exemption No. ____ 4b. Human Subjects Assurance No. None 4c. NIH-defined Phase III Clinical Trial ☒ No ☐ Yes	5. VERTEBRATE ANIMALS ☒ No ☐ Yes 5a. If "Yes," IACUC approval Date 5b. Animal welfare assurance no

6. DATES OF PROPOSED PERIOD OF SUPPORT *(month, day, year—MM/DD/YY)*		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT	
From	Through	7a. Direct Costs ($)	7b. Total Costs ($)	8a. Direct Costs ($)	8b. Total Costs ($)
04/01/03	09/30/03	$100,000	$100,000	$100,000	$100,000

9. APPLICANT ORGANIZATION Name Kinetic Muscles, Inc. Address 1949 East Broadway Road, Suite D Tempe, AZ 85282 Institutional Profile File Number (if known)	10. TYPE OF ORGANIZATION Public: → ☐ Federal ☐ State ☐ Local Private: → ☐ Private Nonprofit For-profit: → ☐ General ☒ Small Business ☐ Woman-owned ☐ Socially and Economically Disadvantaged 11. ENTITY IDENTIFICATION NUMBER EIN 86-1031432 DUNS NO. *(if available)* Congressional District 1
12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE Name Jame B. Koeneman Title President Address 1949 East Broadway Road Tempe, AZ 85282 Tel (480) 557-0448 FAX (480) 55-0449 E-Mail jkoeneman@kineticmuslces.com	13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION Name James B. Koeneman Title President Address 1949 East Broadway Road Tempe, AZ 85282 Tel (480) 557-0448 FAX (480) 557-0449 E-Mail jkoeneman@kineticmuscles.com
14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.	SIGNATURE OF PI/PD NAMED IN 3a. *(In ink. "Per" signature not acceptable.)* JKoeneman — DATE 7/29/02
15. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.	SIGNATURE OF OFFICIAL NAMED IN 13. *(In ink. "Per" signature not acceptable.)* JKoeneman — DATE 7/29/02

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. DO NOT EXCEED THE SPACE PROVIDED.

Stroke (CVA) is the leading cause of disability in the United States and it is estimated that its prevalence will more than double over the next 50 years. Current stroke therapy is labor-intensive and costly. The United States spends $17 billion taking care of stroke survivors. Recently, concentrated, massed practice therapies have been developed that improve function in CVA patients by reversing the effects of "learned nonuse". The objective of this project is to investigate the feasibility of a device that facilitates the administration of massed practice stroke therapy. The long-term objective is to provide a lightweight device for home use that provides motion and biofeedback of desired and undesireable muscle activity. Software controls the function of the device and monitors patient progress and compliance. A pneumatic artificial muscle will be used to provide physical motion. This artificial muscle has many of the properties of human muscle. It is lightweight, flexible and has spring like properties. This project will focuses on treating wrist and finger extensor weakness, however, the concept applies to all areas affected by motor impairment. This Phase I study includes detailed design verification measurements on the device and measures the responses of able bodied test subjects to the treatment protocol.

PERFORMANCE SITE(S) *(organization, city, state)*

Kinetic Muscles, Inc. Tempe, AZ

Barrow Neurological Institute at St. Joeseph's Hospital and Medical Center, Phoenix, AZ

KEY PERSONNEL. See instructions. *Use continuation pages as needed* to provide the required information in the format shown below.
Start with Principal Investigator. List all other key personnel in alphabetical order, last name first.

Name	Organization	Role on Project
Koeneman, James B.	Kinetic Muscles, Inc.	P.I.
Eblen, Cristobel	Southwest Behavioral Health Center	Statistical Consultant
Herring, Donald	Arizona State University	Human Factors, Indus Des.
Koeneman, Edward	Kinestic Muscles, Inc.	Device design & fabrication
Kwasnica, Christina	Barrows Neurological Institue	Physician evaluation
Wendelboe, Douglas	Kinetic Muscles, Inc.	Software & firmware design
Wolf, Steven	Emory University	Therapy consultant

Disclosure Permission Statement. Applicable to SBIR/STTR Only. See instructions. ☒ Yes ☐ No

The name of the principal investigator/program director must be provided at the top of each printed page and each continuation page.

RESEARCH GRANT
TABLE OF CONTENTS

Appendix *(Five collated sets. No page numbering necessary for Appendix.)*

☐ Check if Appendix is Included

Appendices NOT PERMITTED for Phase I SBIR/STTR unless specifically solicited.

Number of publications and manuscripts accepted for publication *(not to exceed 10)* ______

Other items (list)

BUDGET JUSTIFICATION PAGE MODULAR RESEARCH GRANT APPLICATION				
Initial Budget Period	**Second Year of Support**	**Third Year of Support**	**Fourth Year of Support**	**Fifth Year of Support**
$ 100,000.00	$	$	$	$
Total Direct Costs Requested for Entire Project Period				$ 100,000.00

Personnel

During the 6 months of this project, the P.I. will have 30% effort. He will coordinate activities, manage the budget and provide biomechanical analysis. Edward Koeneman will have 30% effort during the 6 months. He will be responsible for hardware design, test and assembly of the devices to be used in the pilot study. Douglas Wendelboe will have 30% effort during the 6 months of the project and will be responsible for programming and data retrieval.

Consortium

Dr. Kwasnica will assist in selecting the clinical participants in the pilot study and participate in the performance and evaluation of the results of the pilot study. Payment to the clinician and caregiver pilot study participants is budgeted to be $14,000. The statistical consulting of Dr. Eblen plus the Human Factors consulting of Donald Herring and Dr. Kwasnica's consulting are estimated to be $10,000. Dr. Steven Wolf from Emory University will consult on concentrated practice, therapy protocols, and evaluation of results at no cost to the grant.

Fixed Fee (SBIR/STTR Only)

None

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
James B. Koeneman	Senior Biomechanics Consultant

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Minnesota, Minneapolis, MN	BSME	1959	Mechanical Engineering
Case Western Reserve University, Cleveland, OH	MS	1966	Bioengineering
Case Western Reserve University, Cleveland, OH	PhD	1970	Structures/Mechanical Design

RESEARCH AND PROFESSIONAL EXPERIENCE

1994 - present	Senior Bioengineering Consultant, BTI Consultants, Tempe, AZ. Assistive Devices, Biomechanics, Development of Composite Materials, Stress Analysis, Failure Analysis.
1994 - 1998	V.P. of Engineering, Orthologic Corporation, Tempe, AZ. Fracture fixation devices, bone growth stimulators.
1984 - 1994	Head of Bioengineering Division, Harrington Arthritis Research Center, Phoenix, AZ. Development of assistive devices, orthopedic implant design and testing, finite element analyses.
1981 - 1983	President, Paulson Medical Devices, Inc., Erie, PA. Development of fracture fixation devices and orthopedic implants.
1974 - 1981	Head of Bioengineering Division, Lord Corporation, Erie, PA. Development and manufacture of orthopedic implants. Composite material development.
1970 - 1974	Bell Telephone Laboratories, Columbus, OH. Development of Piezoelectric switching devices.
1960 - 1964	Reactor Engineer, U.S. Atomic Energy Commission, Argonne, IL.
1959 - 1960	Reactor Engineer, Argonne National Laboratory, Idaho Falls, ID.

PUBLICATIONS

Recipient of 16 patents, co-author of 22 publications and over 115 presentations at technical society meetings. Seven relevant publications listed below:

J.B. Koeneman and J.S. Kaiser, "A Functional Evaluation of the DataHand® Key Entry System User Experience Evaluated By Questionnaire," RESNA, 1994.

J.B. Koeneman and C. Eblen, "A Longitudinal Evaluation of Four-Wheeled Walker: Effects of Experience," Topics in Geriatric Rehabilitation, 8(3)3, 1993.

J.B. Koeneman, "Advanced Materials for Assistive Devices," Topics in Geriatric Rehabilitation, Vol. 8, No. 2, December 1992.

J.B. Koeneman, with others, "A Multi-Dimensional Evaluation of a Four-Wheeled Walker," Assistive Technology, Vol. 4, No. 1, 1992.

J.B. Koeneman, N. Reich, P. Otten, and J. Kaiser, "Clothing for Special Needs; An Information Arena," 10th Annual RESNA Conference, San Jose, CA, 1987.

J.B. Koeneman and M. Phillips, "Composite Materials for Rehabilitation Devices," 10th Annual RESNA Conference, San Jose, CA, 1987.

J.B. Koeneman, "State of the Art of Finite Element Analysis in Orthopaedics," Materials Research Society, Proceedings of Medical Devices and Materials Symposium, 1987.

AWARDS

International Fellow of Biomaterials Science and Engineering; International Union of Societies for Biomaterials Science and Engineering (1999)

Clemson Award for Contributions to the Literature, Society for Biomaterials (1997)

Fellow of Society for Advancement of Material and Process Engineering International (SAMPE) (1992)

Chapter Fellow Award, Society for Advancement of Materials and Process Engineering (SAMPE) (1990)

Engineer of the Year Award, Erie Engineering Society Council (1982)

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.
Photocopy this page or follow this format for each person.

NAME	POSITION TITLE
Steven L. Wolf, Ph.D., FAPTA	Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE (*if applicable*)	YEAR(s)	FIELD OF STUDY
Clark University, Worcester, MA	BA	1965	Biology
Boston University, Boston, MA	MS	1969	Physical Therapy
Emory University, Atlanta, GA	MS	1972	Anatomy
Emory University, Atlanta, GA	PhD	1973	Anat/Neurophysiology
Karolinska Institute, Stockholm, Sweden	Postdoctoral	1973-75	Neurophysiology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

RESEARCH AND PROFESSIONAL EXPERIENCE

1969-70	Instructor, Anatomy and Physiology, Boston University, Boston, MA
1975-88	Principal Investigator, Emory University Rehab. Research & Training Center, Atlanta, GA
1975	Assistant Professor, Dept. of Surgery, Emory University School of Medicine, Atlanta, GA
1975-85	Assistant Professor, Dept. Anatomy, Emory University School of Medicine, Atlanta, GA
1975-78	Assistant Professor, Dept. of Rehab. Med., Emory University School of Medicine, Atlanta, GA
1978-85	Associate Professor, Dept. of Rehab. Med., Emory University School of Medicine, Atlanta, GA
1985-Present	Professor, Dept. of Rehabilitation Medicine, Emory University School of Medicine, Atlanta, GA
1988-2000	Director of Research, Dept. of Rehab. Med., Emory University School of Medicine, Atlanta, GA

HONORS

Marian Williams Research Award, 1980
Georgia Merit Award, Physical Therapy Association of Georgia, 1983
Golden Pen Award, American Physical Therapy Association, 1983
Catherine Worthingham Fellow of the American Physical Therapy Association, 1987
Outstanding Research Contributor to Advancing the Understanding of Biofeedback Mechanisms, Association of Applied Psychophysiology and Biofeedback, 1987
President, Association of Applied Psychophysiology and Biofeedback, 1991-92
Helen J. Hislop Award for Outstanding Contributions to Professional Literature, American Physical Therapy Association, 1993
Award of Excellence, Section on Clinical Electrophysiology, American Physical Therapy Association, 1993
Steven J. Rose Memorial Lectureship, Washington University, St. Louis, Missouri, 1994
Lucy Blair Service Award, American Physical Therapy Association, 1996
First John V. Basmajian Lectureship, International Society of Electrophysiology and Kinesiology, 1996
Section on Geriatrics, APTA, Outstanding published paper award, 1997.
Neurology Section, APTA, Outstanding Researcher Award, 1998.

Dr. Steve Wolf Appreciation Day, February 11, 1998, Warner-Robbins, Georgia: Outstanding Contributions to Rehabilitation in Georgia.
Lester Duplechen Outstanding Faculty Teacher Award, Department of Rehabilitation Medicine, 1999.
Stroke Council, American Heart Association, 1999.
APTA Mary McMillan Lecturer, 2002

SELECTED RELEVANT PUBLICATIONS (from over 200)

Wolf SL, Catlin PA, Ellis M, et al: Assessing the Wolf motor function test as an outcome measure for research with patients post-stroke. Stroke, 2001, in print.

Sathian K, Greenspan A, Wolf SL: Doing it with mirrors - a novel approach to stroke rehabilitation. J. Neural Repair and Neuroscience,14:73-76, 2000.

Wolf SL, Catlin PA, Ellis M, Link A, Morgan B, Piacentino A: Assessing the Wolf motor function test as an outcome measure for research with patients post-stroke. Stroke, 2000, submitted for publication.

Baer HR, Wolf SL: The modified Emory Functional Ambulation Profile: An outcome measure for the rehabilitation of post-stroke gait dysfunction. Stroke, 32:973-979,2000.

Kressig RW, Wolf SL, Sattin RW, O'Grady M, Greenspan A, Curns A, Kutner M: Associations between demographic and functional characteristics to activity-related fear of falling among older adults transitioning to fraily. J Amer Geriatr Soc, 2001, in print.

Griffith, JS Kreutzer, B Pentland (eds), Rehabilitation of the Adult and Child with Traumatic Brain Injury, third edition, FA Davis, Philadelphia, 2000.

Blanton S, Wolf SL: Effectiveness of upper extremity constraint-induced movement therapy on a patient with sub-acute stroke. Physical Therapy, 79:847-853, 1999.

Wolf SL. Catlin PA, Bonner B, Marks M, Weston M: Up-training loading responses in older adults. Applied Psychophysiology and Biofeedback, 24: 179-195, 1999.

Blanton S, Porter L, Smith D, Wolf SL: Strategies to enhance mobility in traumatic brain injured patients. In M. Rosenthal, ER

Wolf SL, Gregor RJ: Exploring unique applications of kinetic analyses to movement in older adults. J. Applied Biomechanics, 15:75-83, 1999.

Blanton SR, Wolf, SL: Effects of constraint-induced movement therapy intervention on individuals with upper extremity hemiparesis. Neurology Report, 1998, 22:164.

Taub E, Wolf SL: Constraint induction techniques to facilitate upper extremity use in stroke patients. Topics in Stroke Rehabilitation, 4:38-61, 1997.

Edgerton VR, Wolf SL, Levendowski DJ: Theoretical basis for patterning EMG amplitudes to assess muscle dysfunction. Medicine and Science Sports and Exercise, 28:744-751, 1996.

Edgerton VR, Wolf SL, Levendowski DJ, Roy RR: Evaluating patterns of EMG amplitudes for trunk and neck mucles of patients and controls. International J. Rehabiltation and Health, 2:1-18, 1996.

Edgerton VR, Wolf SL, Levendowski DJ: Theoretical basis for patterning EMG amplitudes to assess muscle dysfunction. Medicine and Science Sports and Exercise, 28:744-751, 1996.

Wolf SL, Segal RL, Catlin PA, Kantos H, Pate P, Raleigh T, Tschorn J: Determining consistency of elbow joint threshold angle in spastic elbow flexor muscles. Phys. Ther., 76:586-600, 1996.

Wolf SL, Segal RL: Downtraining human biceps-brachii spinal stretch reflexes. J. Neurophysiol., 75:1637-1645, 1996.

Wolf SL, Segal RL, Heter ND, Catlin PA: Contralateral and long latency effects of human biceps brachii stretch reflex conditioning. Exp. Brain Res., 107:96-102, 1995.

Wolf SL, Catlin PA, Blanton S, Edelman J, Lehrer N, Schroeder D. Overcoming limitations in elbow movement in the presence of antagonist hyperactivity. Phys. Ther., 74:35-44, 1994.

Wolf SL, Barton LA: Learned nonuse in the hemiplegic upper extremity. In Gordon WA (ed), Advances in Stroke Rehabilitation. Anover Medical Publishers: Boston, 1993, pp. 79-86.

Wolf SL, LeCraw DE, Barton LA, Jann BB: A comparison of motor copy and targeted feedback training techniques for restitution of upper extremity function among neurologic patients. Phys Ther, 69:719-735, 1989.

Wolf SL, LeCraw DE, Barton LA, Jann BB: Forced use of hemiplegic upper extremities to reverse the effect of learned non-use among chronic stroke and head injured patients. Exp Neurol, 104:125-132, 1989.
Evatt ML, Wolf SL, Segal RL: Modification of human spinal stretch reflexes: Preliminary studies. Neurosci Letters, 105:350-335, 1989.
Wolf SL, Binder-Macleod SA: EMG biofeedback applications to the hemiplegic patient: Changes in upper extremity neuromuscular and functional status. Phys Ther, 63:1393-1403, 1404-1413, 1983.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Christina M. Kwasnica M.D.	**Director of Brain Injury Rehabilitation**

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Arizona Tucson, AZ	BA	1991	Political Science
Northwestern University Medical School Chicago, IL	MD	1995	Medicine

POSITIONS:

Resident Physician Northwestern University Medical School/Rehabilitation Institute of Chicago Department of Physical Medicine and Rehabilitation Chicago, IL 1995-1999

Clinical Instructor and Cognitive Neurology Fellow Northwestern University Alzheimer's Disease Center Departments of Neurology and Physical Medicine and Rehabilitation Chicago, IL 1999-2000

Director of Brain Injury Rehabilitation Barrow Neurological Institute Phoenix AZ 2000-present

PROFESSIONAL AFFILIATIONS:

Diplomate, American Board of Physical Medicine and Rehabilitation

Fellow, American Association of Physical Medicine and Rehabilitation

Diplomate, Association of Academic Physiatrists

AWARDS AND HONORS:

Seabury Foundation Endowed Research Resident- July 1998-June 1999

NIH National Research Service Award Fellowship- F32 NS10858-01 August 1999-August 2000

Sara Baskin Award for Research Excellence- Rehabilitation Institute of Chicago- May, 1999

President's Citation- 62nd Annual Assembly of the American Academy of Physical Medicine and Rehabilitation- for outstanding paper presentation- "Predictors of Ambulation in Stroke Rehabilitation"

RESEARCH PROJECTS ONGOING OR COMPLETED DURING THE LAST THREE YEARS:

Current

Predictors of Ambulation in Stroke Rehabilitation with Dr. Richard Harvey, Rehabilitation Institute of Chicago

Pending

Unilateral Neglect and the Relationship of Measurements with Function

Prior

Bromocriptine in Unilateral Neglect- F32 NS10858-01
NIDRR Stroke Research and Training Center- Rehabilitation Institute of Chicago

PEER REVIEWED PUBLICATIONS:

Kwasnica, CM and Heinemann, A. "Coping with Traumatic Brain Injury: Representative Case Studies," Archives of Physical Medicine and Rehabilitation, April 1994, 384-389.

Grujic, Z, Mapstone, M, Gitelman, D, Weintraub, S, Johnson, N, Hays, A, Kwasnica, CM, Harvey, RL, and Mesulam, M. "Dopamine Agonists Reorient Visual Exploration Away from Neglected Hemisphere," Neurology, December 1998.

Kwasnica, CM. "Unilateral Neglect after Right Hemisphere Stroke- a Review of the Syndrome and Management," Critical Reviews in Physical Medicine and Rehabilitation, accepted for publication December, 2000.

SELECTED RECENT ABSTRACTS AND PRESENTATIONS:

Kwasnica, CM, Harvey, RL, and Mullarkey, C. "Predictors of Ambulation in Stroke Rehabilitation," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November, 2000

Kwasnica, CM, Cherney, L, and Harvey, RL. "Unilateral Neglect and Relationships with Functional Outcomes," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November, 1998.

Kwasnica, CM, Grujic, Z, Mapstone, M, and Harvey, RL. "Bromocriptine Effect on Unilateral Visual Neglect After Right Hemisphere Infarct: A Pilot Study," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November, 1997.

Managing Neglect Syndrome after Stroke: A Complete Experience- Annual Assembly of the American Academy of Physical Medicine and Rehabilitation, Novernber, 1998.

Managing Neglect Syndrome after Stroke: A Complete Experience- Annual Multidisciplinary Stroke Course- Rehabilitation Institute of Chicago, April 1999

Pharmacology of Brain Injury- Rehabilitation Institute of Chicago- December 2000

Non-traumatic Brain Injury- Rehabilitation Institute of Chicago- December 2000

Pharmacologic Approaches to Motor Recovery after Stroke- Annual Multidisciplinary Stroke Course- Rehabilitation Institute of Chicago- April 2000

Atypical Dementias- Grand Rounds- Ingalls Hospital- Chicago, IL- April 2000

Neuroplasticity and Rehabilitation- Grand Rounds- Rehabilitation Institute of Chicago- July 2000

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Douglas E. Wendelboe	Software Consultant; President, Penn Microsystems

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Pennsylvania State University, State College, PA	BS	1972	Electrical Engineering
University of Pennsylvania, Philadelphia, PA	MS	1976	Electrical Engineering

RESEARCH AND PROFESSIONAL EXPERIENCE

1998-Present Software Consultant, BTI Consultants, Tempe, AZ. Design of hardware and software for medical devices

1981-Present President, Penn Microsystems. Consulting on microprocessor-based products. Medical device projects include:

- Hand-held Blood Prothrombin-Time Measuring Device, San Jose, CA, 2000-Present
- Designed and implemented the Automated Calibration and Test System for the Bone Growth Stimulator, Phoenix, AZ, 1999-2000
- Firmware enhancements for an electromagnetic Bone Growth Stimulator, Phoenix, AZ, 1997-1999
- Developed an Automated Active Burn-In System for the Bone Growth Stimulator, Phoenix, AZ, 1996-1997
- Designed and implemented firmware for Nerve Integrity Monitor Instrument, Jacksonville, FL, 1994-1995
- Designed, implemented, and maintained the firmware for a line of Micro-titer Plate Readers, Winooski, VT, 1982-1985
- Designed and implemented the complete firmware for a Pacemaker Systems Analyzer, Winooski, VT, 1980-1981

1977-1981 Senior Associate Engineer, IBM Corp., Essex Junction, VT

1976-1977 Senior Product Engineer, Honeywell Corp., Ft. Washington, PA

1972-1976 Design Verification Software Engineer, UNISYS (Sperry-Univac), Blue Bell, PA

PROFESSIONAL PUBLICATIONS

"Recommended Use of the PL/M Computer Language in Safety-Related Systems," Report for the Nuclear Regulatory Commission, NUREG/CR-6463, June 1996

Co-publisher of the Annual "Arizona High Tech Directory"

Columnist for the "Arizona High Tech Times" newspaper

PROFESSIONAL

IEEE Computers, IEEE Software, IEEE Management, IEEE Biomedical

American Society for Quality

TECHNICAL SKILLS

Languages: Keil C51 w/uVision2, IAR C, PIC-C, 8051, 8x86, 68xx, 68xxx assembler, Microchip PIC, Hitachi H8 assembler, TMS320C54x Algebraic assembler, National Instruments LabWindows/CVI, Microsoft Visual C++, Visual Basic

RTOS: uC/OS-II, QNX, Keil RTX-51, familiarity with VxWorks, Tornado

Microprocessors: Intel 8051, 80251, 8X93x USB, Intel 80x86, 80188, 386EX, 68HC05, 68HC08, 68HC11, 68xxx family, Hitachi 6303, H8S/2134, Microchip PIC16C74, 16C65, ST Micro ST10F167/168

In-Circuit Emulation: Intel ICE 8051, 8085, 80188, 80x86, Nohau EMUL51-PC: 80C552, 89C51RD2, Microchip PIC-Master & others

Peripheral Buses: I²C, CAN v2.0, USB, Motorola SPI, Dallas Semiconductor interfaces

Design Standards: IS)-9001 Design Quality Standards, FDA (97-4179) Medical Device Quality Systems Standards, FDA 510(k), FDA Pre-Market Approval (PMA)

Bus Boards: PC/104 Bus, STD Bus, VME Bus

Logic: SPICE Simulation, Programmable Logic Compilers

Network: TCP/IP, WATTCP

Database: MS SQL7, Oracle, Informix

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Edward J. Koeneman	Consultant

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Arizona State University, Tempe, AZ	BSEET	1992	Electronic Engineering
Arizona State University, Tempe, AZ	MT	1994	Electronic Engineering

POSITIONS

1999-Present	BTI Consultants, Consultant.
1997-1999	Adtron Corp., Mesa, Arizona. Product Manager, Data Storage Devices.
1997	PCI Medical, Phoenix, Arizona. Design Engineer, Medical Electronics.
1995-1997	Prescom Electronics, Mesa, Arizona. Chief Engineer, Contract Electronic Design and Manufacturing.
1988-1995	Harrington Arthritis Research Center, Phoenix, Arizona. Lab Coordinator for Orthopaedic Resident Projects, Mechanical Testing.

PEER REVIEWED PUBLICATIONS

Koeneman, E.J., J.A. Lerman, R.J. Haynes, J.B. Koeneman, W. B. Wong, "A Biomechanical Comparison of Gardner-Wells Tongs and Halo Device Used for Cervical Spine Traction," SPINE, Volume 19, Number 21, pp. 2403-2406, 1994.

Koeneman, E.J., N.R. Crawford, A.G.U. Brantley, C.A. Dickman, "An Apparatus Applying Pure Nonconstraining Moments To Spine Segments In Vitro," SPINE, Volume 20, Number 19, pp. 2097-2100, 1995.

SELECTED PRESENTATIONS

Koeneman, E.J., J.A. Lerman, J.E. Maisel, J.B. Koeneman, "Electromyographic Analysis of the Hockey Slapshot," Presented at 1994 Fall Meeting of the Biomedical Engineering Society.

AWARDS AND HONORS

IEEE Outstanding Student Achievement Award, 1993

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Donald E. Herring	Senior Industrial Design Consultant

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
American University, Washington, DC	BA	1967	Govt. and Public Admin.
Arizona State University, Tempe, AZ	BS	1982	Product Design
Arizona State University, Tempe, AZ	MSD	1993	Human Factors and Design

PROFESSIONAL EXPERIENCE

2001-Present	Senior Industrial Design Consultant, BTI Consultants, Tempe, Arizona
1998-Present	Assistant Professor, Arizona State University, Tempe, Arizona
1997-1999	Proprietor, Redfish Design, Phoenix, Arizona
1994-1997	Assistant Professor, Purdue University, West Lafayette, Indiana
1992-1994	Exhibit and Industrial Designer, Sunbelt Scenic Studios, Inc., Tempe, Arizona
1991-1992	Exhibit Designer, Giltspur Exhibits, Phoenix, Arizona
1982-1989	Senior Project Designer, Mattel Toys, Hawthorne, California
1975	Arizona Real Estate Sales and Brokerage, Phoenix, Arizona
1973	Specialist, United States Treasury Department, Washington, D.C.
1972	Foreman, Athens Paint & Drywall Company, Alexandria, Virginia
1968	OJT Contract Writer, Washington Urban League, Washington, D.C.
1968	Capitol Policeman, United States Capitol Building, Washington, D.C.

PRINCIPAL PROFESSIONAL PUBLICATIONS AND PRESENTATIONS

"Children's Computer Human Factors and Seating Recommendations" (For Our Greatest Future Resource), Natural Resources, 1995 IDSA Design Education Conference Proceedings, Santa Fe, New Mexico, September 1995

"Twenty Years Later: What Are the 11982 Graduates of an Industrial Design Program Doing in the New Millennium?," Gumbo, 2000 IDSA Design Education Conference Proceedings, New Orleans, Louisiana, September 2000

MEMBERSHIPS IN SCIENTIFIC AND PROFESSIONAL SOCIETIES

Human Factors and Ergonomics Society of America
Arizona Chapter Member of the Human Factors and Ergonomics Society of America
Industrial Design Society of America (IDSA)
The Arizona IDSA Chapter Secretary (Founding member and officer)
The Indiana IDSA Chapter Secretary/Treasurer (Resigned, April, 1997)

PATENTS

U.S. Patent 4,787,876 - Toy Musical Play Set, 11/29/88, assigned
U.S. Patent 4,673,373 - Transformable Toy Block, 6/16/87, assigned
U.S. Patent 4,645,471 - Busy Ball Child's Toy, 3/7/85, assigned

AWARDS, SCHOLARSHIPS AND HONOR SOCIETIES

Netherlands Toy of the Year Award to Disney Pots and Pans Band based on Originality, Safety and Suitability, 1988

Second Place Award ($2,000.00) in Mattel's Toy of the Year Contest for the Invention and Development of the Double Dooz Transformers Toy Line, 1986

Nominated for the Mattel Toys Presidents Award for Leading a "Brainstorming Event" with 40 Participants Producing 100 Product Concepts for Presentation in Ten Days, 1985

Mattel $2000.00 Discretionary Award for "The First Innovative Preschool Product Line to Come out of Mattel in Eight Years," 1985

Arizona State University Outstanding Senior Industrial Design, 1982

Honorable Mention ($250.00) in Mattel Toy Design Contest, 1982

Awarded Internship at Mattel Toys, 1982

Phi Kappa Phi National Honor Society, 1982

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow this format for each person. DO NOT EXCEED FOUR PAGES.

NAME	POSITION TITLE
Cristobal Neal Eblen, Ph.D.	Director of Planning, Research and Program Evaluation

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Marist College	BA	1976	Psychology
Marist College	MA	1978	Community Psychology
Arizona State University	Ph.D.	1987	Social Psychology

NOTE: **The Biographical Sketch may not exceed four pages. Items A and B may not exceed two of the four-page limit.**

A. **Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

Post-doctoral Research Fellow (Harrington Arthritis Research Center) 1987-89
Psychologist I (AZ Department of Corrections) 1989-90
Psychologist II (Arizona State Hospital) 1990-91
Research and Statistical Analyst III (AZ Division of Behavioral Health Services) 1991-93
Psychologist II (Southern Arizona Mental Health Center) 1993-96
Psychologist II (AZ Department of Corrections) 1996-97
Research Associate (Community Partnership of Southern Arizona) 1997-2000

B. **Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation.

Eblen, C. & Koeneman, J. (1993). A longitudinal evaluation of a four-wheeled walker: Effects of experience. Topics in Geriatric Rehabilitation, 8, 65-72.

Eblen, C. (1992). Evaluation of assistive devices. Topics in Geriatric Rehabilitation, 8, 6-11.

Eblen, C. & Koeneman, J. (1991). A multi-dimensional evaluation of a four-wheeled walker. Assistive Technology, 3, 32-37.

C. **Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and responsibilities of principal investigator identified above.

N/A

RESOURCES

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

Laboratory:

KMI leases 1,433 square feet of office and laboratory space. Our lab contains the latest in hardware support tools such as: Logic analyzers, analog & digital oscilloscopes; I2C, USB and CAN bus analyzers; Internet server with TCP/IP tools. We also maintain the latest in software compilers, assemblers, simulators, and other software development tools for microprocessors and systems.

We have a complete model shop for the development of prototypes. This includes saws, sanders drill press and a complete supply of hand tools. We have a complete drafting facility.

These facilities are dedicated to the development of the device described in this proposal and to extensions of the design.

Clinical:

All clinical evaluations will be done at the Barrow Neurological Institute (BNI) of St. Joseph's Hospital in central Phoenix. It was first accredited by the Commission on Accreditation of Rehabilitation Facilities (CARF) in 1988. BNI has a state-of-the-art rehabilitation facility and participates in many clinical rehabilitation research studies. Space and equipment for the clinical evaluations will be available for this study.

Animal:

NA

Computer:

Various computer simulation programs such as AutoCAD, Photoshop, Ilustrator, Humanoid, Perception Video Capture Hunamoid run on eight Pentium computers.

Office:

The office has complete facsimile, copying and printing facilities.

Other:

The KMI facility is adjacent to BTI Consultants that provides secretarial and technician support and miscellaneous consulting on an as needed basis.

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of each.

See above.

INTRODUCTION

The comments that follow are in sequential response to the concerns expressed by the reviewers on the summary statement of the previous grant proposal. Their concerns are summarized, followed by our response. Where appropriate and relevant, the responses are numbered or lettered and the narrative page number where the total response can be found is given next. Additions in this proposal are in italics.

Points of Resume and Summary:

*1(Pages 22 - 25,) **Insufficient details about clinical trial protocol.** At the suggestion of the first reviewer we have changed the protocol to involve only able-bodied participants (caregivers and clinicians).*

*2. (Pages 22 - 24) **Need to better focus on design development and demonstration of usability and feasibility.** The study using caregivers and clinicians will measure and record usability, durability, effectiveness of the feedback means, acceptance of the treatment protocols, and safety.*

*3. (Pages 19, 22, 23) **Reliability of the EMG signals.** The variability of the EMG signals within a treatment and between treatments will be measured on able-bodied subjects.*

*4. (Pages 22 - 24) **Rationale for Training.** The questionnaires and focus group response from caregivers and clinicians will help evaluate and refine the treatment protocols.*

*5. (Pages 22, 24, 25) **Patient Safety.** A Data Safety Management Board (DSMB) was established to review protocals, progress reports, and any incidents.*

*6. (Page 24) **Six hours a day may be too long for stroke patients.** Again the response of the trial participants will evaluate this question. If this treatment time is too long, shorter treatment intervals over extended periods of time are also feasible with a take home device.*

*7. (Page 22) **Healthy subjects should be used.** We redesigned the study to follow this suggestion.*

*8 (Page 22) **Determine adverse events.** A DSMB was included in the study to monitor the pilot study.*

<u>Reviewer 1:</u>

*A. (Page 22) **Suggested using normal subjects.** We have changed the pilot study accordingly..*

*B.(Pages 19, 22, 24, 25) **Safety.** We have added more descriptive information on safety features designed into the device, have added a DSMB, and limited the study to normal participants.*

*C.(Page 19) **Force Measurement.** We have described our method of calibration of the force sensors and how torque about the wrist is determined*

*D.(Pages 19) **Thumb considerations.** How the thumb is abducted and how it can be adjusted for each patient is described. Clinician reaction to this method of handling the thumb and the increased tone with wrist extension is sought in the study.*

*E. **Use of block.** Since we are not using stroke patients, this task practice has been deleted.*

*F. **Wolf Motor Function Test.** Deleted. since stroke patients are no longer included.*

*G.(Pages 22, 24, 25)**Safety and Adverse Events.** See 5. and 8. above.*

Reviewer 2:

The comments by reviewer 2 are all good, valid and need to be addressed when the study is applied to patients. Other comments mirrored comments by reviewer 1 that are addressed above.

<u>Reviewer 3:</u> Comments in addition to those of others.

*H. **Number of devices needed.** Six devices are needed. However to have devices under modification while some tests are ongoing, 12 devices will be made. The costs are included in the budget.*

*I.(Pages 22, 24) **Detailed Engineering Characterization of the device.** A task is included to document the detailed engineering characteristics of the device.*

*J.(Pages 6-8) **Need person experienced with EMG.** Dr. Wolf has written over 30 articles involving EMG and has written a book on the subject. In addition he is a past board member of the Electrokineseology Society and is an assoc. editor of JEM.*

<u>Reviewer 4:</u> Comments in addition to those of others.

*K.(Page 23) **Lack of human interface and concern about compliance.** We will be evaluating these concerns.*

*L **Medical insurance coverage?** This Important question is not germane now but will be a target goal evolving from the Phase II study.*

RESEARCH PLAN

A. SPECIFIC AIMS

The **primary purpose** of this project is to improve the restoration of upper extremity physical function of stroke patients by incorporating into one device, the treatment modalities of repetitive practice, and force and electromyographic (EMG) biofeedback. Each of these components may in and of itself demonstrate varying degrees of success in treating stroke patients. The device will assist therapy by supplying increased amounts of information to the physician and therapist while reducing the amount of patient contact time. The device will be adaptable to accommodate the changing paradigm of cerebrovascular accident (CVA) rehabilitation service delivery and to assist in studies designed to refine therapy protocols. The **hypothesis** to be tested is whether it is feasible for this device to *provide a comfortable and safe method of therapy. The first step of sequential hypothesis testing is to demonstrate usability on a wrist and finger joint model. This first step will be deemed feasible and worthy of further exploration if detailed design verification measurements and the responses of normal test subjects indicate the device will be safe and acceptable by patients.*

The specific aims of this proposal are:

1. *Document the device design specifications and the patient safety and hazard analysis.*

2. *Document the response of non-affected people to use of the device.*
3. *Refine display methods, software protocols, and patient-device interactions.*

B. BACKGROUND AND SIGNIFICANCE

Many people have movement disabilities caused by disease or injury. Among the causes are cerebrovascular accident or stroke (CVA), traumatic brain injury, multiple sclerosis, spinal cord injury and Parkinson's disease. This project focuses on stroke; however the results will have application to other causes of movement disability. Stroke is the leading cause of disability in the United States with at least 700,000 new cases each year [1-3]. Over half of these people have residual physical disability. Current stroke therapy is labor-intensive and costly. Often insurance does not cover the cost of full therapy. One estimate is that the United States spends $30 billion per year to take care of stroke survivors. Seventeen billion dollars of this cost is direct medical expenditures and thirteen billion dollars represent an indirect cost due to lost productivity [3]. Another estimate is that the total direct and indirect costs of stroke are $43.3 billion per year [3]. The number of strokes is projected to increase because of the increase in the over 50 "baby boom" population. Also, new pharmaceutical treatments for stroke are projected to increase the number of patients surviving a stroke and increase the percentage of stroke survivors requiring rehabilitation. Therefore, it is not surprising that a recent estimate indicates the prevalence of stroke will more than double over the next 50 years [2].

Because of health care reimbursement reductions, therapy time for stroke patients has been significantly decreased. Currently, a majority of time spent in therapy post-stroke concentrates on helping a patient adapt to their disability by teaching toileting skills and transfers. A consequence of this treatment is the emergence of, "learned nonuse" that hinders the restoration of available function [2]. Most current rehabilitation therapies are administered on a spaced basis. Recently, concentrated therapies have been developed that improve function in

CVA patients by reversing the effects of "learned nonuse"[4]. Animal studies suggest that learned nonuse is established immediately after the initial organic damage. A patient is punished for trying to use the affected limb and is rewarded for using other parts of the body. Over time, healing of the organic damage occurs but the suppression of use learned in the acute phase remains in force [4]. As discussed by Taub [4], many of the therapies that have been shown to be effective in restoring function involve massed practice. Physical Therapy training techniques were used by Bach-y-Rita [5,6] and Franz, Scheetz, and Wilson [7]. Significant improvement in limb function was obtained in chronic CVA patients. Training techniques based on EMG biofeedback improved motor ability of chronic CVA patients, as demonstrated in studies by Wolf [8,9], Basmajian [10, 11], and Balliet [12]. Repetitive concentrated practice produced large therapeutic effects for lower limb function [13, 14, 15]. Taub (2,32) has systematically studied a variation of forced use of hemiplegic extremities, originally described by Wolf (31,35,36). Taub has labeled this therapy Constraint-Induced (CI) Movement Therapy [2, 32]. His group has shown positive results in controlled randomized studies [16]. Some of these experiments compared several massed therapy techniques and all showed very large increases in limb use over the treatment period.

Two very sophisticated robot systems are being developed for treatment and evaluation of CVA patients [1, 17]. These devices have shown some effectiveness in treatment of CVA patients and have developed very useful data for understanding recovery mechanisms; however, the current cost of these systems precludes their widespread clinical use [18].

Other studies show that measured EMG can be used to trigger neuromuscular electrical stimulation in restoring function to CVA patients [26, 27, 28, 29]. However, the discomfort of surface neuromuscular stimulation significantly limits the clinical implementation of this modality for persons with hemiplegia [34]. EMG biofeedback treatment of stroke patients has also shown some success [30, 31, 12, 8]. This treatment uses surface electrodes to capture the electrical activity of a selected muscle group. An electronic unit converts the signals into visual or audio information for the patient. This information is used by the patient to augment or decrease muscle activity.

A device that has a venerable history in supplying motion to assistive devices is the <u>pneumatic artificial muscle</u>. The artificial muscle exhibits many of the properties of human muscle. The device consists of an expandable internal bladder, e.g., a rubber tube, surrounded by a braided shell. When the internal bladder is pressurized, it expands radially against the braided shell. The pressure on the inside of the braid causes it to contract. Braided finger traps used to hold fingers on traction devices contract radially when pulled. The **<u>air muscle</u>** works in the same manner only in the opposite direction, i.e., increasing the diameter causes it to shorten. Like human muscle, the device has spring-like characteristics, is flexible, and is lightweight. The force-deflection characteristics can be made similar to those of human muscle. This type of device was first used in the 1950's for powered braces [19, 20]. Pressurized air canisters or accumulators that are recharged by air compressors supply air. Major advantages of the air muscle are its flexibility and ease of adaptation to address the specific loss of function exhibited by a patient. This type of device is often referred to as the McKibben Artificial Muscle. The device has three times the pull force of an air piston of the same cross sectional area. **The potential utility of this device resides in its <u>unique</u> combination of attributes: low cost, light-weight, low profile, and low noise operation**. The device has not been used extensively, because it has been applied in the wrong applications and has suffered from the lack of engineering in critical areas. Research on the application of the air muscle has been revived by the University of Washington [21, 22, 23, 24, 25]. The Shadow Organization in England uses the air muscle to operate biped and multiped robots [33].

C. PRELIMINARY STUDIES

The labor-intensive and long treatment times of forced practice make effective rehabilitation expensive. A promising approach to providing a lightweight, low-cost stroke therapy device is a system that synergistically

combines three modes of feedback that individually have been shown to be effective (visual presentation of desired motion, resistive-force of wrist flexor muscles and EMG activity of the extensor muscles). We have constructed a prototype of an air muscle powered therapy device for the fingers and wrist that has the adaptability to be used in current treatment modalities and also in the refinement of rehabilitation methods. Figure 1 is a drawing of the device. An air muscle is attached to the proximal forearm. Activation of the air muscle rotates a bar that extends the wrist and fingers and operates *a modified Watt six-bar* mechanism that extends the fingers. Wrist extension position is measured by a potentiometer that is incorporated in the device pivot. Resistance to extension is measured by force sensitive resistors (FSRs). Thus the FSR output is a measure of the resistance of finger and wrist flexor muscles. *The FSRs are calibrated after each device is assembled. A load cell is inserted between the activation bar on the mechanism and muscle. The mechanism is fixed in six different degrees of flexion-extension. The ou put of the FSRs is compared to the load cell output. The torque about the wrist at each wrist position is calculated by multiplying the muscle force by the distance to the line of action of the air muscle. Closely spaced surface electrodes measure wrist extensor EMG activity. The location of the EMG electrodes is determined for each patient by the therapist. The skin is rubbed 20 times with alcohol soaked gauze pads. The EMG output is used to measure the relative recruitment of selected extensor muscles and used to feedback the information to the patient to reinforce correct recruitment. Session to session variation in EMG values are recorded but we do not believe they will be a primary indicator of patient progress.*

<u>Wrist and Finger Motion</u>

The air muscle drives the fingers and wrist into extension by moving a mechanical linkage. The linkage is designed to move the fingers and wrist in a spiral fashion. Excessive force on the hand is prevented in several ways. A micro-compressor was chosen that has a maximum output pressure of 28 psi. This limits the maximum force supplied by the air muscle. The air muscle is a very compliant drive with the maximum force output at the fully flexed position where the stretch reflex resistance of the flexor muscles is minimum. As extension proceeds, the stretch reflex increases resistance to motion. If a large resistance is encountered during extension, the air muscle stretches and limits the range of motion. Since spastic flexor muscles are velocity sensitive, the velocity of actuation was chosen to be 5 degrees per second with no loading. With the weight of a flaccid hand this rate decreases to 3.8 degrees per second and with mild resistance the rate is 2.7 degrees per second. Experiments by Richard Herman showed only small increases in muscle tone occurred for very spastic hemiplegics due to velocity at rates below 6 degrees per second [40]. The rate in the KMI device is physically controlled by the volume capacity of the micro-compressor and the resistance in the pneumatic circuits. To prevent excessive extension of the wrist, a physical stop is also provided that limits motion of the activation bar at 60 degrees of wrist extension. A safety panic switch that releases the air pressure is also provided on a tether and is placed close to the subject's non-treating hand. An orthoplast® thumb splint is provided with the device. The fitting clinician can adjust the amount of abduction appropriate for a particular patient.

A microprocessor controls the activation of the air muscle by operating the microcompressor and air valves. Wrist position is displayed as a bar graph on the LCD. The changing goal for active wrist motion is displayed as a line on the graph. One line of multi-color light emitting diodes (LEDs) indicates the degree of flexor resistance torque as measured by the force sensitive resistors. A second line of LEDs indicates the EMG activity of the wrist or finger extensors. The microcompressor, air valves, microprocessor, and the LCD are in a plastic box that sits on a table during therapy sessions. A coiled cable assembly that contains the electrical wires and air hose connects the box to the activation device. This system is a self-contained, mobile device that provides visual feedback of wrist and finger position, EMG extensor activity and wrist flexor resistive torque. The firmware in the microprocessor has been designed to be well-structured using object-oriented programming techniques. Use of these techniques yields more reliable code having fewer discrepancies and problems. Each of the object components was tested separately (component testing). When the firmware was integrated with

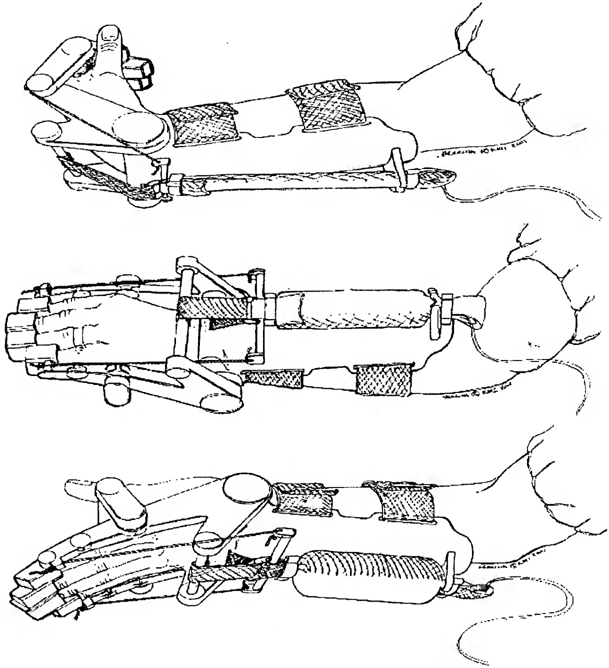
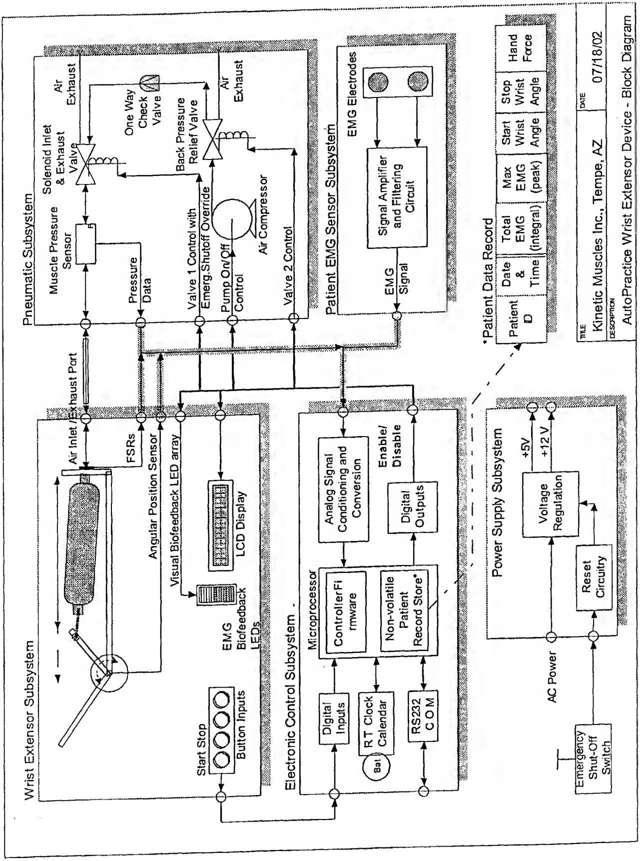


Figure 1 Therapy Device in Flexion, Neutral and Extension; Shrouding, LEDs and Control Box not shown for Clarity


Pneumatic Subsystem
Muscle Pressure Sensor
Solenoid Inlet & Exhaust Valve
Air Exhaust
One Way Check Valve
Back Pressure Relief Valve
Air Exhaust
Pressure Data
Valve 1 Control with Emerg.Shutoff Override
Pump On/Off Control
Air Compressor
Valve 2 Control
Patient EMG Sensor Subsystem
EMG Electrodes
Signal Amplifier and Filtering Circuit
EMG Signal
*Patient Data Record
Patient ID
Date & Time
Total EMG (integral)
Max EMG (peak)
Start Wrist Angle
Stop Wrist Angle
Hand Force
TITLE
Kinetic Muscles Inc., Tempe, AZ
DATE
07/18/02
DESCRIPTION
AutoPractice Wrist Extensor Device - Block Diagram
Air Inlet / Exhaust Port
FSRs
Angular Position Sensor
Visual Biofeedback LED array
LCD Display
EMG Biofeedback LEDs
Start Stop
Button Inputs
Wrist Extensor Subsystem
Electronic Control Subsystem
Analog Signal Conditioning and Conversion
Enable/ Disable
Digital Outputs
Microprocessor
ControllerFirmware
Non-volatile Patient Record Store*
Digital Inputs
RT Clock Calendar
Bat
RS232 COM
Power Supply Subsystem
+5V
+12 V
Voltage Regulation
Reset Circuitry
AC Power
Emergency Shut-Off Switch

the electronic hardware, the complete system was tested (system integration testing). Finally, the operation of the complete device was validated and verified for function by comparing to the design requirements established at the project beginning. The essence of the design requirements is described in this proposal. A block diagram of the system is shown in Figure 2. The real-time clock/calendar is powered by a battery mounted on the printed circuit board when the power is off. The clock maintains the time and date continuously. Records of patient use, active range of motion, extensor resistive torque, and EMG activity are recorded with a time stamp in a non-volatile serial EEPROM memory device. Data is kept safe, even when no power is applied to the memory. These records can be downloaded to a Windows application on the therapist's personal computer. The results are sorted by participant and tabular and graphical displays made available for viewing.

H. EXPERIMENTAL DESIGN AND METHODS

Device Characterization

The purpose of this experiment is to characterize the pneumatic muscle. The characterization will be done by inflating a muscle thus contracting it, adding a sequence of loads and measuring the displacements of the muscle. This is repeated for different pressures of inflation. The experiment will include the testing of the passive force-length properties of the muscles, plugged and unplugged muscles and the reproducibility of muscles of the same type and length. In addition, full engineering characterization of the fully assembled device will be done.

Pilot Study

A pilot study of able-bodied participants will be conducted to determine the usability, safety and feasibility of using this device on stroke patients.

Data Safety Monitoring Board (DSMB) – This board will be established to review the progress of the study with a special interest in participant safety. Dr. Kwasnica, Dr. Wolf, Kay Wing, and Deborah Taylor will be on the board. They will review participant protocols, progress reports and any incident reports.

Participant Population – Five clinicians who treat stroke patients and five caregivers of stroke patients will be recruited. The clinicians will have a minimum of three years experience in treating stroke patients.

Evaluation --Deborah Taylor and Kay Wing, both licensed physical therapists will administer the program. The therapist will explain the operation and purpose of the device. A brochure describing the device and contact information will be provided the participant. The therapist will then place the EMG electrodes on the patient and attach them to the device. The therapist will demonstrate several treatments of the device. The device will be removed and the patient asked to attach the device and start treating without any help. The participants will be required to return after one week and at the end of two weeks for completion of questionnaires regarding acceptability of the device and evaluation of features. The participants will be asked their impression of the device weight and bulkiness, their fatigue during therapy, the effectiveness of the LED and LCD feedback methods, the reliability of the device and they will be asked to provide suggestions. Ratings will be on an ordinal scale.

Protocol – The participant is instructed to try to extend the wrist when a beep is heard. The EMG activity of the wrist extensors and the motion of the wrist are recorded in the memory of the device and displayed for the participant. The participant will be instructed to use the device for at least 6 hours a day, although more treatment is allowed. The treatments do not have to be continuous. The participanat can start and stop the device at any time. The first 2 hours will emphasize EMG and joint position feedback. During the second 2 hours the flexor resistance torque from the flexors will be used as the feedback signal to help the patient reduce any flexor spasticity. The final 2 hours of therapy will have both extensor EMG and flexor resistance torque as

achieved at the beginning of a day and at the end of each day is recorded in memory. This information will provide us with accurate information about participant compliance. The memory of the device will be downloaded onto a PC in the clinic. A summary chart graphically displaying the number of hours of use a day by the participant, the range of motion and the active range of motion by day will be displayed and the charts printed for the participant file.

Data Analysis - Measures: There are three types of data collected in this study:

(1) *The number of hours of use per day by the participant. This is a measure of compliance with treatment.*

(2) *Recording, Displaying and Reporting of Functional Measures such as range of motion, EMG Biofeedback and flexor resistive muscle tone.*

(3) *Participant acceptance of the device as recorded in questionnaires and a final Focus Group.*

Evaluation

Participant acceptance of the device and suggested improvements will be entered into the design control system for the device for evaluation. Correlations will be calculated between reported compliance and actual hours of use.

The device will be considered acceptable and feasible if participant compliance is sufficient and the response to the questionnaires indicates that the device is useable and considered safe.

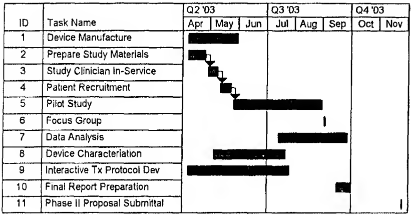
Limitations - *While the numbers of minority and ethnic people in this study preclude statistically significant comparisons, the main purposes of this study are to refine the protocol and the device for a Phase II study and to investigate feasibility, acceptance and safety of this therapeutic device.*

Design Issues – The sensitivity of the EMG measurement to forearm motion and relative motion of muscles with respect to skin will be examined. The repeatability of placement of the electrodes from use to use will also be evaluated. Skin sensitivity to the pressure of the device or type of material will be examined.

Project Plan – *Three tasks will begin at the beginning of the project. Manufacture of the study devices will begin, the documentation to be provided to study participants will begin preparation, and development of innovative interactive treatment firmware will begin. Participant information kits will be sent to them describing the purpose and protocol of the study. Follow-up phone calls will be made to answer any questions and ascertain their willingness to participate in the study. Just before beginning the study, an extensive in-service session will be conducted for the therapists that will be conducting the patient training. Task 5 is the therapy portion of the study. Two clinician and two caregiver participants will begin treatment at the start of Task 5. After one week they will return for completion of questionnaires and debriefing. Then one week is scheduled for adjustment of the devices and firmware based on participant input. Then the three remaining clinicians and three caregivers will be given devices for one week of treatment. After their return and completion of questionnaires three weeks is scheduled for making adjustments in the devices and firmware. Then the two groups of two will return for another week of treatment. This week is followed by one week for*

adjustments and then the final group comes in for the beginning of one week of treatment. At the end of the study, a Focus Group will be held to have interaction between the participant therapists and caregivers in evaluating the device and providing further suggestions. A report of the Focus Group will document the participant's opinions of usability and safety of the device. Concurrent with the participant evaluations, performance characterization of the device, update of the hazard analysis and adjustments to the firmware and displays will be made. A final report addressing the feasibility of the device, device changes suggested by the results, and protocol changes suggested for the Phase II study will be prepared. Assuming feasibility is demonstrated, an application for Phase II funding will be prepared for December 1, 2003, submission.

Table I Gantt Chart



The **deliverables** *of this Phase I study are: (1) a complete characterization of the device performance and hazard analysis, (2) refined displays, donning and doffing procedures and other device features that make the device user friendly, (3) the documented opinions of caregivers and clinicians as to usability, acceptance, and safety of the device.*

The feasibility of using this device in a Phase II study involving stroke patients will be determined by the safety and usability conclusions.

E. HUMAN SUBJECTS

Involvement of Human Subjects: The purpose of the device under evaluation in this proposal is to facilitate the application of concentrated practice for stroke patients. Numerous studies, most notably by Taub and Wolf, have provided this therapy through one-on-one contact with physical therapists. In all of these studies there is no reason to believe that this intervention provides selective benefits (or limitations) based upon gender or racial attributes. In this study the gender and minority status will be recorded and reported for all participants. The numbers are so small that little meaningful statistical conclusions can be made although physiological and functional performance will be reported for these categories. Children less than 18 years of age are excluded because an immature nervous system may respond differently to this therapy than a mature one and the low number of young patients available for this short study.

Human Research Material: *Participants will be in two groups. Group I will be clinicians that have treated stroke patients for a minimum of three years. The identity of participants will be protected. Participants in this trial will receive codes to protect their identity throughout the study.*

Recruitment of subjects: *The clinician participants will be recruited by the two physical therapists that are familiar with this device (Kay Wing and Deborah Taylor). The caregivers of stroke patients will be recruited by Dr. Kwasnica, Kay Wing, and Deborah Taylor.*

Potential Risks: The physical risk involved with using this device is overextending a joint and causing soft tissue damage. *To control this risk the range of motion of the mechanism is limited to the physiological range of motion of a normal person. To protect against overload of spastic muscles or contractures, the amount of force the device can provide is limited. A panic button is provided that removes load and shuts the device down.* Another risk is fatiguing the patient and causing anxiety. The risks involved with use of EMG electrodes are skin irritation. A control on this risk is that the participant has the right to drop out of the study at any time.

Minimization of Risk: The risk of overstretching a joint is controlled in several ways. There is a physical stop incorporated in the device that prevents wrist extension over 60°degrees of extension. If the wrist is stopped by an obstruction, the force is limited by the low stiffness of the air muscle actuator. Also, if the torque measured by the extension bar exceeds 8 newton meters (the resistive torque of the finger and wrist flexors), the air is exhausted and the device shut down. A panic button is also provided for easy access by the unaffected hand that will also exhaust the air muscle and shut the device down if the patient is feeling any discomfort, fatigue or anxiety.

Reasonableness of Risk: As noted above, effective means of controlling the risks are designed into the device. When one realizes that the eventual potential benefit to stroke patients can be substantially enhanced function in real world activities and improved quality of life beyond that achieved during the early rehabilitation interval, the risks are not significant.

FDA Approval: It is our opinion that this device is not a significant risk device and that only IRB approval is required. We will submit the protocol, a description of the device, a patient consent form, and an evaluation of the hazards involved in use of the device and how we are controlling these hazards to the IRB.

F. VERTEBRATE ANIMALS

Not applicable.

G. LITERATURE CITED

1. H.I. Krebs, B.T. Volpe, M.L. Aisen, N. Hogan, "Increasing Productivity and Quality of Care: Robot-aided Neuro-rehabilitation", Journal of Rehabilitation Research and Development, Vol. 37, No. 6, Nov/Dec, 2000, PP 630-652.

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H. CONTRACTUAL ARRANGEMENTS

Dr. Wolf is participating at no cost with the anticipation that this study will lead to a device that is supportive of the treatments being studied in the EXCITE trial.

The applicant organization and St. Joseph's Medical Center/ St. Joseph's Medical Center are prepared to establish in writing the required contractual agreements whereby the clinical institutions will provide physician and therapist services as described in this proposal. The cost of providing these services is included in the budget of this proposal.

I. CONSULTANTS

An Advisory Board for the project will provide advice and guidance on clinical issues, engineering, and product development. The members of the Advisory Board are:

- Dr. Steven Wolf, Ph.D., Professor of Rehabilitation Medicine at Emory University. Dr. Wolf is the principal investigator of a randomized national clinical trial to explore the effect of forced use therapy on patients who have sustained a stroke. He will be advising on the treatment and evaluation protocols and provide general guidance on the treatment of stroke patients.
- Deborah Koeneman has a MS degree in Bioengineering from ASU. She has worked for the Food and Drug Administration in regulation of Medical Devices. She currently is Director of Regulatory Affairs for OrthoLogic Corporation. She will consult on clinical trial, regulatory, and quality assurance issues.
- Don Herring, an Assistant Professor of Industrial Design at ASU, will consult on human factors, industrial design, and attachment design.
- Cristobel Eblen, Ph.D., Cris is a psychologist with experience in designing patient evaluation studies and questionnaires and performing statistical analyses.

EMORY
UNIVERSITY
SCHOOL OF
MEDICINE

Center for Rehabilitation Medicine
Department of Rehabilitation Medicine

July 22, 2002

Mr. James B Koeneman, President
Kinetic Muscles, Inc.
1949 East Broadway Road
Suite D
Tempe, AZ 85282

Dear Jim:

I have read your revised SBIR proposal, "Development of a Massed Practice Stroke Therapy Device"(1 R43 HD41805-01A) regarding the application of your combined force feedback, EMG biofeedback, and pneumatic muscle instrumentation to facilitate improved movement and function in the wrists and digits of patients who have sustained a stroke but in whom movement initiation into extension exists. I believe you have responded admirably to the reviewers comments and that the decision to first field test your device using able-bodied individuals, is a wise one.

As you know, I have spent considerable time researching criteria for the use of EMG biofeedback applied to the upper extremities of patients after stroke. I have also done considerable work in the area of "forced use" or "constraint induced movement therapy" among stroke patients and currently am PI on the NIH funded EXCITE (EXtremity Constraint Induced Therapy Evaluation) national clinical trial. I will be more than honored to serve as a consultant to your project. I am very concerned that the potential to use multi-modal (muscle and force) physiological feedback be made optimal and researched with extreme vigor. I believe that your device will assist in the delivery of excellent product development and well-performed research. I am most impressed by your staff's commitment to this project.

Good luck with your efforts. Having read your proposal, I believe you have addressed all the reviewer comments comprehensively. If I can assist in any way during the final preparation of this proposal, please feel free to call upon me.

Steven L. Wolf

STEVEN L. WOLF, Ph.D., FAPTA, PT
Professor, Department of Rehabilitation Medicine
Professor of Geriatrics, Department of Medicine
Associate Professor, Department of Cell Biology
Director, Program in Restorative Neurology (PROREN)
Emory University School of Medicine

Emory University School of Medicine
1441 Clifton Road NE
Atlanta, Georgia 30322

Tel 404.712.5507
Fax 404.712.5895

The Robert W. Woodruff Health Sciences Center
An equal opportunity, affirmative action university

Barrow Neurological Institute®
St. Joseph's Hospital and Medical Center

June 1, 2001

To whom it may concern:

This letter shall serve as a letter of support for the Small Business Innovation Research grant titled "Development of a Massed Practice Stroke Therapy Device." I am pleased to be asked to participate in the opportunity to engineer a device that may assist patients in applying the principles of massed practice in their stroke recovery.

As Director of Brain Injury Rehabilitation at Barrow Neurological Institute, I have the background to be able to participate in such research. I am looking forward to collaboration in this study.

Sincerely,
C. Kwasnica MD
Christina Kwasnica M.D.
Attending Physiatrist
Barrow Neurological Institute
St. Joseph's Hospital & Medical Center
Phoenix, AZ 85013

Barrow Neurological Institute®
St. Joseph's Hospital and Medical Center
CHW

350 West Thomas Road
Phoenix, AZ 85013
602 406 3000 Telephone

March 29, 2001

James B. Koneman, Ph.D.
1937 East Broadway Road
Tempe, AZ 85282-1701

Dear Dr. Koneman:

The research project "Development of a Massed Practice Stroke Therapy Device" as submitted by BTI Consultants has the full administrative support and approval of our institution.

Catholic Healthcare West Arizona, dba St. Joseph's Hospital and Medical Center, is familiar with federal subcontract policies. Upon negotiation of a NIH subcontract, our institution will fully comply with those policies if the grant is awarded to BTI Consultants.

Sincerely,

Toby L. Anchie

Toby L. Anchie, R.N., MAEd
Executive Director, Research & Development

CHECKLIST

TYPE OF APPLICATION *(Check all that apply.)*

☐ NEW application. *(This application is being submitted to the PHS for the first time.)*

☒ SBIR Phase I ☐ SBIR Phase II: SBIR Phase I Grant No. ______ ☐ SBIR Fast Track

☐ STTR Phase I ☐ STTR Phase II: STTR Phase I Grant No. ______ ☐ STTR Fast Track

☒ REVISION of application number: 1R43HD041805-01A1

(This application replaces a prior unfunded version of a new, competing continuation, or supplemental application.)

☐ COMPETING CONTINUATION of grant number: ______

(This application is to extend a funded grant beyond its current project period.)

☐ SUPPLEMENT to grant number: ______

(This application is for additional funds to supplement a currently funded grant.)

INVENTIONS AND PATENTS *(Competing continuation appl. and Phase II only)*

☐ No

☐ Yes. If "Yes," ☐ Previously reported ☐ Not previously reported

☐ CHANGE of principal investigator/program director.

Name of former principal investigator/program director: ______

☐ FOREIGN application or significant foreign component.

1. PROGRAM INCOME ***(See Instructions.)***

All applications must indicate whether program income is anticipated during the period(s) for which grant support is request If program income is anticipated, use the format below to reflect the amount and source(s).

Budget Period	Anticipated Amount	Source(s)
	0	

2. ASSURANCES/CERTIFICATIONS ***(See Instructions.)***

The following assurances/certifications are made and verified by the signature of the Official Signing for Applicant Organization on the Face Page of the application. Descriptions of individual assurances/ certifications are provided in Section III. If unable to certify compliance, where applicable, provide an explanation and place it after this page.

•Human Subjects; •Research Using Human Embryonic Stem Cells• •Research on Transplantation of Human Fetal Tissue •Women and Minority Inclusion Policy •Inclusion of Children Policy• Vertebrate Animals• •Debarment and Suspension; •Drug- Free Workplace *(applicable to new [Type 1] or revised [Type 1] applications only)*; •Lobbying; •Non-Delinquency on Federal Debt; •Research Misconduct; •Civil Rights (Form HHS 441 or HHS 690); •Handicapped Individuals (Form HHS 641 or HHS 690); •Sex Discrimination (Form HHS 639-A or HHS 690); •Age Discrimination (Form HHS 680 or HHS 690); •Recombinant DNA and Human Gene Transfer Research; •Financial Conflict of Interest (except Phase I SBIR/STTR) •STTR ONLY: Certification of Research Institution Participation.

3. FACILITIES AND ADMINSTRATIVE COSTS (F&A)/ INDIRECT COSTS. See specific instructions.

☐ DHHS Agreement dated: ______ ☒ No Facilities And Administrative Costs Requested.

☐ DHHS Agreement being negotiated with ______ Regional Office.

☐ No DHHS Agreement, but rate established with ______ Date ______

CALCULATION* *(The entire grant application, including the Checklist, will be reproduced and provided to peer reviewers as confidential information.)*

a. Initial budget period: Amount of base $ ______ x Rate applied ______ % = F&A costs $ ______

b. 02 year Amount of base $ ______ x Rate applied ______ % = F&A costs $ ______

c. 03 year Amount of base $ ______ x Rate applied ______ % = F&A costs $ ______

d. 04 year Amount of base $ ______ x Rate applied ______ % = F&A costs $ ______

e. 05 year Amount of base $ ______ x Rate applied ______ % = F&A costs $ ______

TOTAL F&A Costs $ ______

*Check appropriate box(es):

☐ Salary and wages base ☐ Modified total direct cost base ☐ Other base *(Explain)*

☐ Off-site, other special rate, or more than one rate involved *(Explain)*

Explanation *(Attach separate sheet, if necessary.)*:

4. SMOKE-FREE WORKPLACE ☒ Yes ☐ No *(The response to this question has no impact on the review or funding of this application.)*

Section E Human Subjects (addendum)

Inclusion Plans for Women, Minorities & Children

The targeted enrollment in the Pilot Study is in the following table. Children less than 18 years of age are excluded because an immature nervous system may respond differently to this therapy than a mature one and the low number of young patients available for this short study. See Involvement of Human Subjects on p. 24.

Targeted/Planned Enrollment Table

This report format should NOT be used for data collection from study participants.

Study Title: Pilot Study of Usability, Safety and Feasibility of Stroke Therapy Device

Total Planned Enrollment: 10

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	1	0	1
Not Hispanic or Latino	6	3	9
Ethnic Category Total of All Subjects*	7	3	10
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	2
White	6	2	8
Racial Categories: Total of All Subjects *	7	3	10

*The "Ethnic Category Total of All Subjects" must be equal to the "Racial Categories Total of All Subjects."

Data & Safety Monitoring Plan

Adverse events will be monitored during the clinical study to determine if there are any device-related adverse effects. As outlined on page 25 of this proposal, anticipated potential adverse device effects include overextension of the wrist and/or fingers, patient fatigue, and skin irritation under EMG electrodes. All anticipated adverse device effects will be reported to the Data Safety Monitoring Board (see p. 22) as they occur and a summary of all events will be supplied to the IRB and the NIH at the conclusion of the study.

Sent by e-mail 9/30/02

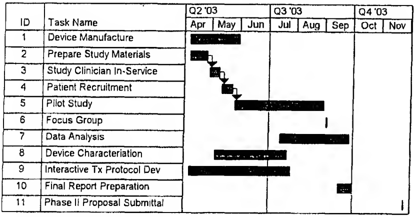
An *unanticipated adverse device effect* is any serious adverse effect on health or safety, any life-threatening problem or death caused by, or associated with a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Investigators will be required to submit reports of unanticipated adverse device effects KMI. NIH and the reviewing IRB as soon as possible and no later than 10 working days after the investigator first learns of the effect.

KMI will submit results of evaluations of unanticipated adverse device effects to the FDA, NIH, IRB, and participating investigators within 10 working days after receiving notice of effect.

justments and then the final group comes in for the beginning of one week of treatment. At the end of the study, a Focus Group will be held to have interaction between the participant therapists and caregivers in evaluating the device and providing further suggestions. A report of the Focus Group will document the participant's opinions of usability and safety of the device. Concurrent with the participant evaluations, performance characterization of the device, update of the hazard analysis and adjustments to the firmware and displays will be made. A final report addressing the feasibility of the device, device changes suggested by the results, and protocol changes suggested for the Phase II study will be prepared. Assuming feasibility is demonstrated, an application for Phase II funding will be prepared for December 1, 2003, submission.

Table I Gantt Chart



The **deliverables** *of this Phase I study are: (1) a complete characterization of the device performance and hazard analysis, (2) refined displays, donning and doffing procedures and other device features that make the device user friendly, (3) the documented opinions of caregivers and clinicians as to usability, acceptance, and safety of the device.*

The feasibility of using this device in a Phase II study involving stroke patients will be determined by the safety and usability conclusions.

E. HUMAN SUBJECTS

Involvement of Human Subjects: The purpose of the device under evaluation in this proposal is to facilitate the application of concentrated practice for stroke patients. Numerous studies, most notably by Taub and Wolf, have provided this therapy through one-on-one contact with physical therapists. In all of these studies there is no reason to believe that this intervention provides selective benefits (or limitations) based upon gender or racial attributes. In this study the gender and minority status will be recorded and reported for all participants. The numbers are so small that little meaningful statistical conclusions can be made although physiological and functional performance will be reported for these categories. Children less than 18 years of age are excluded because an immature nervous system may respond differently to this therapy than a mature one and the low number of young patients available for this short study.

Human Research Material: *Participants will be in two groups. Group I will be clinicians that have treated stroke patients for a minimum of three years. The identity of participants will be protected. Participants in this trial will receive codes to protect their identity throughout the study.*

_cruitment of subjects: *The clinician participants will be recruited by the two physical therapists that are familiar with this device (Kay Wing and Deborah Taylor). The caregivers of stroke patients will be recruited by Dr. Kwasnica, Kay Wing, and Deborah Taylor.*

Potential Risks: The physical risk involved with using this device is overextending a joint and causing soft tissue damage. *To control this risk the range of motion of the mechanism is limited to the physiological range of motion of a normal person. To protect against overload of spastic muscles or contractures, the amount of force the device can provide is limited. A panic button is provided that removes load and shuts the device down.* Another risk is fatiguing the patient and causing anxiety. The risks involved with use of EMG electrodes are skin irritation. A control on this risk is that the participant has the right to drop out of the study at any time.

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F. VERTEBRATE ANIMALS

Not applicable.

G. LITERATURE CITED

1. H.I. Krebs, B.T. Volpe, M.L. Aisen, N. Hogan, "Increasing Productivity and Quality of Care: Robot-aided Neuro-rehabilitation", Journal of Rehabilitation Research and Development, Vol. 37, No. 6, Nov/Dec, 2000, PP 630-652.

Principal Investigator/Program Director (Last, first, middle):

DETAILED BUDGET FOR INITIAL BUDGET PERIOD DIRECT COSTS ONLY	FROM 7/01/04	THROUGH 6/30/05

PERSONNEL (*Applicant organization only*)					DOLLAR AMOUNT REQUESTED (*omit cents*)		
NAME	ROLE ON PROJECT	TYPE APPT. (*months*)	% EFFORT ON PROJ.	INST. BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Richard Herman, MD	Principal Investigator	12	20.0	100,000	20,000	4,800	24,800
Vassia Roulia	Res Monitor	12	30.0	55,000	16,500	3,960	20,460
Therapist	Evaluator	12	50.0	61,167	33,584	8,060	41,644
Res. Coordinator	Clin. Res Coordinator	12	50.0	73,840	36,920	8,861	45,781
			0.0	0	0	0	0
SUBTOTALS →					87,004	20,881	107,884

CONSULTANT COSTS		0
EQUIPMENT (*Itemize*)		0
SUPPLIES (*Itemize by category*)		0
TRAVEL Nat'l Stroke Mtg		1,500
PATIENT CARE COSTS	INPATIENT	
	OUTPATIENT	0
ALTERATIONS AND RENOVATIONS (*Itemize by category*)		
OTHER EXPENSES (*Itemize by category*)		
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		$109,384
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
	FACILITIES AND ADMINISTRATIVE COSTS	0
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD (*Item 7a, Face Page*) →		$109,384
SBIR/STTR Only: FEE REQUESTED		

Form Approved Through 05/2004

OMB No. 0925-0001

Department of Health and Human Services
Public Health Services

Grant Application

Do not exceed character length restrictions indicated.

LEAVE BLANK—FOR PHS USE ONLY		
Type	Activity	Number
Review Group		Formerly
Council/Board (Month, Year)		Date Received

1. TITLE OF PROJECT *(Do not exceed 56 characters, including spaces and punctuation.)*

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION ☐ NO ☐ YES
(If "Yes," state number and title)
Number: Title:

3. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR

New Investigator ☐ **No** ☐ **Yes**

3a. NAME *(Last, first, middle)*

3b. DEGREE(S)

3c. POSITION TITLE

3d. MAILING ADDRESS *(Street, city, state, zip code)*

3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT

3f. MAJOR SUBDIVISION

3g. TELEPHONE AND FAX *(Area code, number and extension)*
TEL: FAX:

E-MAIL ADDRESS:

4. HUMAN SUBJECTS RESEARCH
☐ No
☐ Yes

4a. Research Exempt ☐ No ☐ Yes
If "Yes," Exemption No.

4b. Human Subjects Assurance No.

4c. NIH-defined Phase III Clinical Trial ☐ No ☐ Yes

5. VERTEBRATE ANIMALS ☐ No ☐ Yes

5a. If "Yes," IACUC approval Date

5b. Animal welfare assurance no.

6. DATES OF PROPOSED PERIOD OF SUPPORT *(month, day, year—MM/DD/YY)*

From	Through

7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD

7a. Direct Costs ($)	7b. Total Costs ($)
[illegible]	[illegible]

8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT

8a. Direct Costs ($)	8b. Total Costs ($)

9. APPLICANT ORGANIZATION
Name
Address

Institutional Profile File Number (if known)

10. TYPE OF ORGANIZATION
Public: → ☐ Federal ☐ State ☐ Local
Private: → ☐ Private Nonprofit
For-profit: → ☐ General ☐ Small Business
☐ Woman-owned ☐ Socially and Economically Disadvantaged

11. ENTITY IDENTIFICATION NUMBER

DUNS NO.
Congressional District

12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE
Name
Title
Address

Tel: FAX:
E-Mail:

13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Name
Title
Address

Tel: FAX:
E-Mail:

14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

SIGNATURE OF PI/PD NAMED IN 3a.
(In ink. "Per" signature not acceptable.)

DATE

15. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF OFFICIAL NAMED IN 13.
(In ink. "Per" signature not acceptable.)

DATE

Principal Investigator/Program Director (Last, first, middle):

DETAILED BUDGET FOR INITIAL BUDGET PERIOD DIRECT COSTS ONLY	FROM 7/01/04	THROUGH 6/30/05

PERSONNEL (*Applicant organization only*)					DOLLAR AMOUNT REQUESTED (*omit cents*)		
NAME	ROLE ON PROJECT	TYPE APPT. (*months*)	% EFFORT ON PROJ.	INST. BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
James Koeneman	Principal Investigator	12	30.0	120,000	36,000	8,460	44,460
Edward Koeneman	Engineering	12	30.0	100,000	30,000	6,900	36,900
Robert Schultz	Indust Des.	12	30.0	38,000	11,400	2,622	14,022
Pat Jacobson	Ops Mfg	12	20.0	80,000	16,000	3,680	19,680
TBN	ASU Intern	12	50.0	30,000	15,000	0	15,000
	SUBTOTALS →				72,400	13,202	85,602

CONSULTANT COSTS Statitician	1,500
EQUIPMENT (*Itemize*) 20 devices @ 3500, Dell650 Workstation 1800	71,800
SUPPLIES (*Itemize by category*) Software licenses, upgrades $1000 Electronics disks, cartridges $500 Electrodes & Supplies $500 Lab Supplies $2500	4,500
TRAVEL Nat'l Stroke Mtg	1,500
PATIENT CARE COSTS — INPATIENT	
PATIENT CARE COSTS — OUTPATIENT	4,700
ALTERATIONS AND RENOVATIONS (*Itemize by category*)	
OTHER EXPENSES (*Itemize by category*) IRB Charges $2200	2,200
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD	**$171,802**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS 109K	161,888
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD (*Item 7a, Face Page*) →	**$** 333 690
SBIR/STTR Only: FEE REQUESTED 7%	21,168

Facilities and Administrative (F&A) Costs

Indicate the applicant organization's most recent F&A cost rate established with the appropriate DHHS Regional Office, or, in the case of for-profit organizations, the rate established with the appropriate PHS agency cost advisory office. If the applicant organization is in the process of initially developing or renegotiating a rate, or has established a rate with another Federal agency, it should, immediately upon notification that an award will be made, develop a tentative F&A cost rate proposal. This is to be based on its most recently completed fiscal year in accordance with the principles set forth in the pertinent DHHS Guide for Establishing Indirect Cost Rates, and submitted to the appropriate DHHS Regional Office or PHS agency cost advisory office. F&A costs will NOT be paid on construction grants, grants to Federal organizations, grants to individuals, and conference grants. Follow any additional instructions provided for Research Career Awards, Institutional National Research Service Awards, Small Business Innovation Research/Small Business Technology Transfer Grants, foreign grants, and specialized grant applications.

Personnel

Name	Role	Appt. type	%Effort	Inst Sal.	Requested	Fringe	Subtotal	*Totals*
Richard Herman, MI	PI	12	20	100,000	20,000	4,800	24,800	
Vassia Roulia	Res Monitor	12	30	55,000	16,500	3,960	20,460	
Therapist	Evaluator	12	50	67,167	33,584	8,060	41,644	
Res Coordinator	Clinical Res Coor	12	50	73,840	36,920	8,861	45,781	
Evaluator	WMFT/kin/fMRI	12	0	30,000	0	0	0	
Recruiter/Trainer	Rec/Train	12	0	35,000	0	0	0	
Kay Wing	Consult	12	0	60,000	0	0	0	
	Consult	12	0	80,000	0	0	0	
Personnel subtotal					***87,004***	***20,881***	***107,884***	***107,884***
					Fringe % GT	0 240		